UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2017
Or
o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

Commission file number 001-36080

OPHTHOTECH CORPORATION
(Exact name of registrant as specified in its charter)

Delaware	**20-8185347**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
One Penn Plaza, 35th Floor **New York, NY**	**10119**
(Address of principal executive offices)	(Zip Code)

(212) 845-8200
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.001 par value	The Nasdaq Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. o Yes ☒ No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. o Yes ☒ No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. ☒ Yes o No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). ☒ Yes o No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of “large accelerated filer,” “accelerated filer,” “smaller reporting company,” and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐ Accelerated filer x Non-accelerated filer ☐ Smaller reporting company ☐ Emerging growth company ☐
(Do not check if a smaller reporting company)

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). o Yes ☒ No

As of June 30, 2017, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was approximately $91.8 million, based on the closing price of the registrant's common stock on June 30, 2017.

The number of shares outstanding of the registrant's class of common stock, as of February 27, 2018: 36,151,332

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report incorporates by reference information from the definitive Proxy Statement for the registrant's 2018 Annual Meeting of Shareholders, which is expected to be filed with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2017.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "goals," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- the potential benefits of our business plan and strategy to develop Zimura® (avacincaptad pegol) in orphan ophthalmic indications and age-related retinal diseases and potentially expand our product pipeline, including through collaborative gene therapy research programs;
- our ability to in-license or acquire additional products, product candidates or technologies to treat ophthalmic diseases and the timing, costs, conduct and outcome of preclinical development or clinical trials we undertake for these newly acquired assets;
- our expectations related to our use of available cash;
- our estimates regarding expenses, future revenues, capital requirements and needs for, and ability to obtain, additional financing;
- the timing, costs, conduct and outcome of our ongoing and planned clinical trials, including statements regarding the timing of the initiation of and completion of enrollment in such trials, and the costs to obtain and timing of receipt of initial results from, and the completion of, such trials;
- the timing of and our ability to obtain marketing approval of our product candidates, and the ability of our product candidates to meet existing or future regulatory standards;
- the potential advantages of our product candidates;
- the rate and degree of potential market acceptance and clinical utility of our product candidates, if approved;
- our estimates regarding the potential market opportunity for our product candidates;
- the potential receipt of revenues from future sales of our product candidates, if approved;
- our sales, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for the manufacture of our product candidates;
- our intellectual property position;
- the impact of existing and new governmental laws and regulations; and
- our competitive position.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and our stockholders should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the "Risk Factors" section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

PART I

Item 1. Business

Overview

We are a science-driven biopharmaceutical company specializing in the development of novel therapies to treat ophthalmic diseases, with a focus on age-related and orphan retinal diseases. Our multi-track strategy is to leverage our clinical experience and retina expertise to develop therapies for large market, age-related retinal diseases, where unmet medical needs remain for these patients, and for orphan eye diseases with a focus on underserved patients, and to utilize a disciplined business development approach to obtain additional products, product candidates and technologies in these disease areas. We believe that there are advantages to pursuing drug development for orphan indications, including the potential for regulatory exclusivity, the potential for clinical trials with smaller sample sizes and the potential for accelerated development timelines. Our team has significant ophthalmic drug development experience and deep relationships with global ophthalmology thought leaders. We have an extensive network of ophthalmic clinical trial sites, having worked with over 250 sites worldwide. We believe that the combination of these factors, together with our experience in designing and executing IND-enabling studies and clinical trials for eye diseases, and specifically back of the eye diseases, provide us a competitive advantage.

We are developing Zimura® (avacincaptad pegol), our complement C5 inhibitor, for dry and wet forms of age-related macular degeneration, or AMD, which is a disorder of the central portion of the retina, known as the macula, that may result in loss of central vision, and autosomal recessive Stargardt disease, or STDG1, which is an orphan inherited retinal disease that also may result in loss of central and peripheral vision. In connection with our Stargardt clinical trial, which we recently initiated, we have expanded our network of thought leaders and clinical trial sites for orphan ophthalmic indications to include leading research university hospitals around the world, where patients with orphan retinal diseases are often referred.

We are actively engaged in extensive business development efforts to identify, evaluate and potentially obtain rights to and develop additional therapeutic and gene therapy product candidates that would complement our strategic goals and leverage our competitive advantages. We believe that our strategy will provide multiple potential opportunities to bring ophthalmic therapies to market.

Zimura

Based on our Zimura development experience to date, as well as scientific literature in the field, we believe there is a strong rationale to pursue the development of our C5 complement inhibitor, Zimura, in multiple ophthalmic diseases. Zimura is a chemically-synthesized, pegylated RNA aptamer. Aptamers are short molecules made up of a single stranded nucleic acid sequence or an amino acid sequence that bind molecular targets with high selectivity and specificity. We have multiple clinical development programs for Zimura ongoing or planned to initiate by the end of 2018. Our ongoing and planned clinical trials for Zimura, all of which are designed to obtain data to guide potential future development efforts, include the following:

- **OPH2003 (geographic atrophy (GA) secondary to dry AMD)**: an ongoing, randomized, double–masked, sham controlled, multi-center Phase 2b clinical trial evaluating the safety and efficacy of Zimura monotherapy in patients with geographic atrophy, or GA, secondary to dry AMD. GA, the end stage of dry AMD, is a disease characterized by retinal cell death and degeneration of retinal tissue.

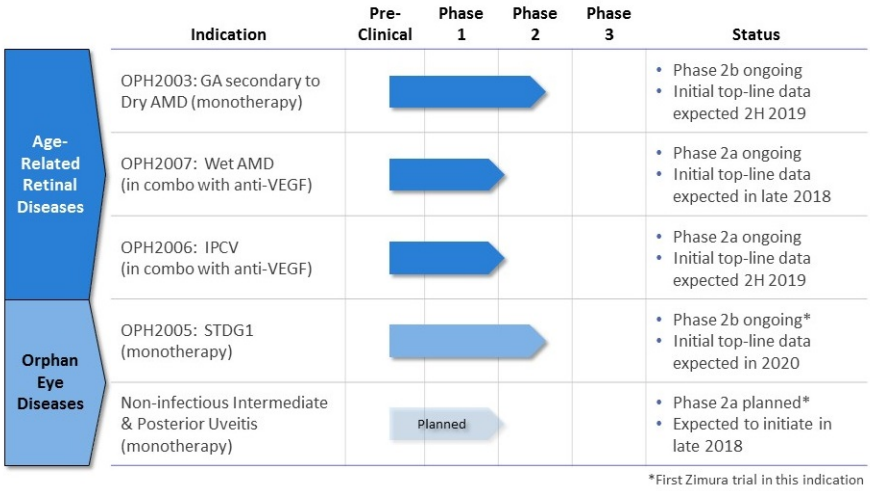
- **OPH2007 (wet AMD)**: an ongoing, randomized, dose-ranging, open-label, multi-center Phase 2a clinical trial of Zimura in combination with the anti-vascular endothelial growth factor, or anti-VEGF, agent Lucentis® (ranibizumab) for the treatment of wet AMD in patients who have not previously been treated with anti-VEGF agents, referred to as treatment-naïve patients. Wet AMD is characterized by the presence and growth of abnormal new blood vessels under and through the retina.

- **OPH2006 (IPCV)**: an ongoing, randomized, dose-ranging, open-label Phase 2a clinical trial of Zimura in combination with the anti-VEGF agent Eylea® (aflibercept) for the treatment of idiopathic polypoidal choroidal vasculopathy, or IPCV, in patients who have not responded to Eylea monotherapy. IPCV is an age-related retinal disease involving the choroidal vasculature characterized by the presence of polypoidal lesions, which leads to vision loss. We are at a very early stage of site initiation and patient recruitment for this trial.

- **OPH2005 (autosomal recessive Stargardt disease (STGD1))**: an ongoing, randomized, double-masked, sham controlled, multi-center Phase 2b clinical trial evaluating the safety and efficacy of Zimura monotherapy for the treatment of autosomal recessive Stargardt disease, referred to as STGD1. We are at a very early stage of patient recruitment for this trial.

- **Non-infectious intermediate and posterior uveitis**: a planned open-label Phase 2a clinical trial of Zimura monotherapy for the treatment of non-infectious intermediate and posterior uveitis, a rare inflammatory disease of the back of the eye.

The following table summarizes the current status of these ongoing and planned Zimura development programs:



On-going Business Development and Pipeline Expansion Activities

Since early 2017, we have been engaged in extensive business development efforts. Without limiting any option, the principal focus of this plan, based on our deep expertise and experience in ophthalmic drug development, has been to actively explore obtaining rights to additional products, product candidates and technologies to treat ophthalmic diseases, particularly those in the back of the eye. We evaluated a large number of assets and platforms during 2017 and continue to actively review assets, platforms and other compelling ophthalmology opportunities that would complement our strategic goals. We have considered multiple opportunities over the last several months, including in-licensing, obtaining rights to products, product candidates or technologies, acquisitions, mergers and reverse mergers. Our selection criteria are based on several factors. In general, we are looking for:

- compelling science;
- an identified unmet medical need based on the current standard of care;
- a meaningful commercial opportunity based on existing treatment options and treatment options known to be in development; and
- areas where we believe we can apply our competitive advantages.

Based on our work to date, among the novel technologies we have evaluated, we believe that gene therapy solutions may be particularly well-suited for our strategy as potential treatments for both orphan and age-related eye diseases. We remain committed to being opportunistic and will consider other compelling opportunities that may emerge.

Eye Diseases

Eye diseases can be caused by many factors and can affect both the front or back of the eye. In its most extreme cases, eye disease can result in blindness. In the developed world, the major diseases that result in blindness are those affecting the retina and optic nerve, including AMD, diabetic retinopathy and glaucoma. These diseases deprive patients of their sight and, as a result, their ability to live independently and perform daily activities. Any improvement in vision, or even a slowing of the rate of progression of vision loss, has a tremendous impact on the quality of life of people with impaired vision. There are also many other eye diseases that may be less common but still represent an unmet medical need, particularly orphan diseases associated with a genetic mutation that lead to retinal degeneration and vision loss. We believe these disease areas present several potential opportunities for ophthalmic drug development.

Age Related Macular Degeneration

AMD is a disease characterized by progressive degenerative abnormalities in the macula, a small area in the central portion of the retina responsible for sharp vision. AMD is characteristically a disease of the elderly and is the leading cause of blindness in individuals over the age of 50 in developed countries. There are two forms of AMD, dry AMD and wet AMD. Dry AMD is characterized by degeneration of the macula, and with continued progression over multiple years, may ultimately result in atrophy of the central retina associated with progressive central vision loss. By contrast, wet or neovascular AMD, which is characterized by the growth of abnormal new blood vessels under and into the retina, although less prevalent, is more likely to cause sudden, often substantial, loss of central vision.

According to AMD Alliance International, approximately 10 million people in the United States and 30 million people worldwide suffer from some form of AMD. AMD Alliance International estimates that dry AMD accounts for 85% to 90% of all AMD cases. Based on U.S. Census Bureau data, we estimate that over the next two decades in the United States the number of people aged 55 or older is expected to increase by approximately 36% and the number of people aged 65 and older is expected to increase by approximately 69%. We expect that this increase in the number of elderly people will result in a significant increase in the number of cases of both dry AMD, including cases of GA, and wet AMD in the United States. In addition to having a devastating effect on patients, AMD also has a significant impact on the economy. According to a 2010 study sponsored by AMD Alliance International, the annual direct healthcare system costs of visual impairment worldwide due to AMD were estimated at approximately $255 billion.

Dry AMD

Dry AMD is a significant cause of moderate and severe loss of central vision, affecting vision in both eyes in most patients. Although dry AMD is the most common form of AMD, there are no U.S. Food and Drug Administration, or FDA, or European Medicines Agency, or EMA, approved therapies to treat this condition. In dry AMD, thinning of the retinal pigment epithelial, or RPE, cells in the macula develops, along with other age-related changes to the adjacent retinal and choroidal tissue layers. The RPE is a layer of cells within the retina on which photoreceptors are dependent. Dry AMD is typically associated with yellow–white dots or deposits under the RPE, known as drusen. Unlike in wet AMD, there is an absence of abnormal new blood vessel growth, or neovascularization, in dry AMD. The presence of drusen, in the absence of pathological neovascularization, is critical for making the diagnosis of dry AMD in patients over 50 years of age. GA, the end-stage of dry AMD, can result in progressive and chronic degeneration of the retina characterized by variable thinning and dysfunction of retinal tissue.

The progression of visual outcomes for patients with dry AMD is variable. Most patients experience mild to moderate loss of visual function, manifesting in blurring of central vision in the affected eye, as a result of progressive degeneration of the light–sensitive photoreceptor cells in the macula. There are two instances in which visual loss from dry AMD may lead to severe vision loss:

- *Geographic Atrophy.* The progression of dry macular degeneration with age can result in a severe form of retinal degeneration called GA, which typically leads to profound and irreversible vision loss. GA is readily diagnosed during retinal examination using standard diagnostic instruments utilized by ophthalmologists. GA appears as abrupt and deep levels of macular tissue loss. It has sharp margins of characteristic degeneration compared to surrounding healthier macular tissue, resulting in progressive and chronic degeneration of the retina characterized by variable thinning and dysfunction of retinal tissue. A comprehensive epidemiology study published in 2004 in Archives of Ophthalmology estimates that there are approximately 1 million people in the United States with GA.

- *Conversion to Wet AMD.* Dry AMD progresses to the wet form of the disease in approximately 10% – 15% of patients, leading to more rapid and further visual loss. A study on the burden of AMD published in 2006 in the

peer reviewed journal *Current Opinion in Ophthalmology*, estimated that 1,250,000 people in the United States suffer from wet AMD. In addition, AMD Alliance International reports that approximately 200,000 new cases of wet AMD arise each year in the United States.

The absence of treatment options for dry AMD represents an area of urgent unmet medical need, and a major public health concern for the rapidly increasing elderly population.

Wet AMD

Wet AMD occurs when new and abnormal blood vessels proliferate under or within the retina. These abnormal new blood vessels originate beneath the retina, in a layer called the choroid, and invade into the overlying retinal layers. This abnormal new blood vessel growth is generally referred to as pathological angiogenesis. In the context of wet AMD, pathological angiogenesis is associated with both the development of neovascular cells and the accumulation of other cell types and altered tissue. The pathological neovascular tissue in wet AMD is called the choroidal neovascular complex or choroidal neovascularization. Choroidal neovascularization, or CNV, and adjacent and contiguous areas of blood and altered tissue are referred to as a lesion.

Abnormal new blood vessels tend to be fragile and often bleed and leak fluid into the macula. Untreated, new blood vessel growth and associated leakage typically lead to retinal distortion and rapid vision loss. The end stage of the disease features scarring with irreversible destruction of the macula. Approximately 90% of wet AMD cases involve subfoveal choroidal neovascularization, which is blood vessel growth directly under the central portion of the macula, known as the fovea. We plan to enroll patients with active subfoveal wet AMD in our wet AMD trials.

The current standard of care for wet AMD is administration of anti–VEGF monotherapy agents by intravitreal injection. Anti-VEGF agents prevent VEGF from binding to its natural receptor on endothelial cells in the abnormal new blood vessels, thereby inhibiting further abnormal new blood vessel growth and leakage associated with wet AMD. The FDA has approved the anti-VEGF agents Lucentis, Eylea and Macugen for the treatment of wet AMD. The FDA also has approved photodynamic therapy with Visudyne (PDT) as a treatment for patients with wet AMD. In addition, although approved by the FDA as a cancer therapy, the anti–VEGF drug Avastin® (bevacizumab) is used off–label to treat wet AMD. Lucentis is an antibody fragment derived from the same full-length antibody from which Avastin was derived.

AMD and the Complement System

The causes of AMD are not completely understood. In addition to advanced age, there are environmental and genetic risk factors for developing AMD including ocular pigmentation, dietary factors, a positive family history for AMD, high blood pressure and smoking. A body of recent scientific literature suggests that complement system activation may contribute to the pathogenesis and progression of the disease.

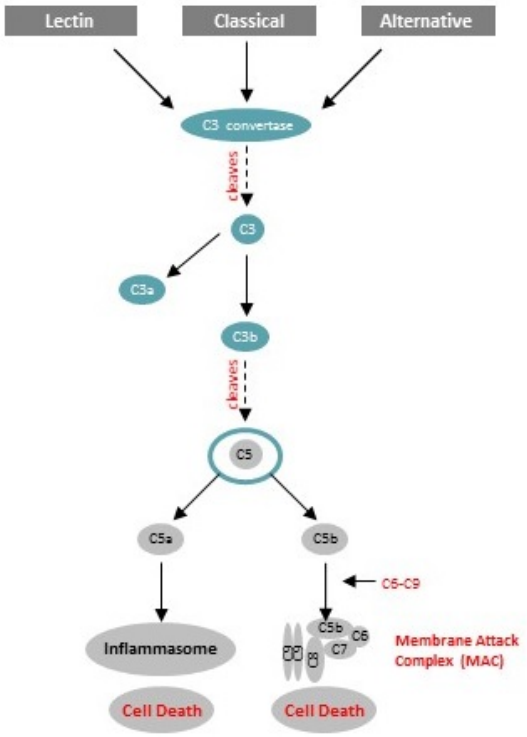
The complement system consists of a series of proteins that are involved in the defense of the host body against infectious agents, or pathogens, and other foreign proteins. The complement system modulates a variety of immune and inflammatory responses to these pathogens and foreign proteins. Under normal circumstances, complement proteins, together with antibodies and white blood cells, act beneficially to protect the host body by removing the pathogens and foreign proteins, together with other cellular debris. The complement system is generally tightly regulated, achieving the proper balance of activation and inhibition depending on the host body's requirements. Poorly regulated or aberrant activation of the complement system, without a balanced or proportional inhibition of complement proteins, may result in a variety of pathological conditions. Activation of the complement system has been implicated in drusen formation. Moreover, complement system activation has also been implicated in preclinical laser-induced CNV models.

The complement system is generally activated via one of three biological pathways:

- the classical pathway, which is activated by an antibody-pathogen protein complex;
- the alternative pathway, which is activated by the binding of a specific complement protein, C3b, to a pathogen or pathogen fragment; and
- the lectin pathway, which is activated by the binding of a specific blood, or serum, protein called mannose-binding protein, to carbohydrates present on the surface of pathogens.

These pathways eventually converge with the generation of an enzyme known as C3 convertase. C3 convertase cleaves, or separates, a serum protein called C3, into C3a and C3b. C3b is an important element of the body's immune response, as it binds to pathogens and makes them susceptible to destruction by white blood cells. C3b also cleaves complement protein C5. The cleavage of C5 results in the formation of the terminal complement fragments C5a and C5b. C5a has been found to prime RPE cells for inflammasome activation in the presence of waste products from the visual cycle. Inflammasomes are intracellular protein structures that lead to cell death. C5b, in combination with serum proteins C6, C7, C8 and C9, leads to the generation of C5b-9, or membrane–attack complex, or MAC. MAC accumulation in RPE cells leads to mitochondrial damage and cellular dysfunction, eventually leading to cell death. A study published in the *American Journal of Ophthalmology* in 2002 described the presence of MAC in post-mortem human donor eyes with dry AMD and GA.

A simplified illustration of the complement system appears below:



VEGF Inhibition and Complement

Avastin, Lucentis and Eylea, on average, all improve the visual outcomes in eyes with wet AMD. A study published in *Ophthalmology*, which is the official journal of the American Academy of Ophthalmology, in 2013, however, found that, despite maximal therapy with monotherapy intravitreal anti-VEGF agents, after one year of treatment the majority of patients do not achieve significant visual gain (defined as a gain of 15 or more ETDRS letters). Furthermore, in another study, an increase in dosage or treatment frequency did not lead to additional efficacy and it appears that a "ceiling" for the effect of anti-VEGF therapy may have been reached. In addition, in a third-party clinical trial, after one year of treatment with an anti-VEGF agent, approximately 18% to 22% of newly diagnosed wet AMD patients lost additional vision, defined as the loss of the ability to read one or more ETDRS letters. In a separate study published in *Ophthalmology* in 2014, approximately one- fifth of the patients who had received anti-VEGF therapy developed GA within two years of treatment. The authors concluded that anti-VEGF therapy may play a role in the development of atrophy. In a follow-up publication from 2017, the authors found that following five years of anti-VEGF treatment, the cumulative incidence of GA had increased to 38% and concluded that the development of GA was common after five years of anti-VEGF treatment for wet AMD.

Complement factor H, or CFH, is a complement regulatory protein that down-regulates complement system activation in the eye. In a recent study published in the *Journal of Clinical Investigation* in 2017, a direct relationship between VEGF and CFH was demonstrated, where the presence of VEGF up-regulated CFH levels and down-regulated complement system activation. In RPE cells, inhibition of VEGF lead to a decrease in CFH levels. In this study, mice that received anti-VEGF

treatment showed a marked decrease in VEGF and CFH leading to increased MAC levels, suggesting that inhibition of VEGF with anti-VEGF agents may contribute to complement system activation. Further, in patients with wet AMD, aqueous humor samples collected from the front of the patients' eyes 48 hours after intravitreal injection of Avastin demonstrated a decrease in VEGF levels but an increase in the levels of complement proteins C3a, C4a, and C5a as compared to the levels seen prior to Avastin treatment.

Taken together, these findings indicate that although inhibition of VEGF has a potent effect on CNV leakage, inhibition of VEGF may also potentially contribute to complement system activation by reducing CFH levels and therefore limit the full therapeutic potential of anti-VEGF therapy in wet AMD patients.

Idiopathic Polypoidal Choroidal Vasculopathy

Idiopathic polypoidal choroidal vasculopathy, or IPCV, is an age-related disease of the choroid characterized by the presence of polypoidal vascular lesions with or without an associated vascular network. In IPCV, leakage under the RPE, subretinal hemorrhage and RPE detachment are common. When leakage or hemorrhage occurs in the macular region, central vision loss occurs. IPCV is often diagnosed as a variant of wet AMD, although it may occur without the associated neovascularization. IPCV is more prevalent in certain populations with pigmented eye color, including Asian populations. Although anti-VEGF therapy is typically administered for IPCV, multiple studies demonstrate that anti-VEGF therapy may not be as effective in IPCV as it is in wet AMD. For many of the same reasons as those described above under "VEGF Inhibition and Complement," we believe that complement inhibition when added to anti-VEGF therapy may improve the results of anti-VEGF therapy for patients with IPCV.

Stargardt Disease

Stargardt disease is a rare, inherited genetic disease that causes progressive damage to the macula and retina, leading to loss of central vision in children and adolescents. The autosomal recessive form of the disease is referred to as STGD1. An inherited trait is referred to as autosomal recessive when the subject must inherit the trait from each parent for the condition to manifest. Multiple sources, including the National Eye Institute and Genetics Home Reference, both of which are affiliated with the U.S. National Institutes of Health, estimate the prevalence of Stargardt disease to be between 1 in 8,000 and 1 in 10,000, implying an overall prevalence of 32,000 to 41,000 affected persons in the United States, with, we believe, at least as many affected persons in Europe. STDG1, the most common type of Stargardt disease, is caused by mutations in the ABCA4 gene. For STGD1, a subject must inherit a mutation to the ABCA4 gene from each parent. There are currently no therapies approved by the FDA or EMA to treat Stargardt disease. The FDA has recognized Stargardt as an orphan disease, with several treatments in development having received orphan product designation from the FDA.

Visual Cycle Waste Accumulation and MAC Accumulation

STGD1 is caused by mutations in the ABCA4 gene, which is responsible for making a protein that helps to clear byproducts resulting from the visual cycle from inside photoreceptor cells in the eye. With a defective copy of the ABCA4 protein, these waste byproducts accumulate in the RPE. Waste byproducts that accumulate in the RPE are referred to as bisretinoids. We believe that the accumulation of bisretinoids in RPE cells leads to activation of the complement system. One of the final products of all three complement pathways is MAC. In RPE cells, MAC is normally cleared by lysosomes, which are organelles within cells responsible for waste degradation and disposal. Bisretinoid accumulation leads to lysosomal dysfunction, potentially preventing the clearance of MAC. MAC accumulation also negatively impacts energy production by the mitochondria inside RPE cells. Bisretinoid and MAC accumulation may lead to RPE cell deterioration and contribute to the loss of photoreceptor cells, leading to a decrease in vision over time.

In April 2017, *Proceedings of the National Academy of Sciences*, or PNAS, published a study reporting on the effects of complement system modulation in the RPE of a mouse model of Stargardt disease. Injection of a recombinant adeno-associated virus containing the coding sequence for a protein that inhibits complement system activation, Crry, into an albino ABCA4 mutant mouse model led to a two-fold reduction in the accumulation of bisretinoids and a 30% increase in the number of photoreceptor nuclei at one year. The study findings indicate that the inhibition of complement activation may lead to healthier RPE cells, which in turn are better capable of processing bisretinoids in the albino ABCA4 mutant mice when compared to untreated mice. Research performed at Duke University and published in a paper appearing in 2013 in *Investigative Ophthalmology & Visual Science* demonstrated that RPE cell damage resulting from the combination of complement system activation and visual cycle waste was far more damaging than either component individually *in vitro*. When complement factor C5 was blocked, there was a significant improvement in RPE cell viability *in vitro*. Based on the data from these *in vitro* and *in vivo* experiments, we believe molecules involved in inhibition or regulation of complement system activation and MAC accumulation are prime targets for therapeutic intervention in STGD1.

Zimura

We are developing our product candidate Zimura for the treatment of four ophthalmic conditions: GA secondary to dry AMD, wet AMD, IPCV and STDG1. Zimura is a chemically-synthesized, pegylated RNA aptamer. Aptamers are short molecules made up of a single stranded nucleic acid sequence or an amino acid sequence. The specific three-dimensional structure of an aptamer, which results from its specific sequence, allows it to bind molecular targets with high selectivity and specificity. Zimura is designed to target and inhibit the complement protein C5. We believe that Zimura binds to C5 and inhibits it from cleaving into the terminal fragments, C5a and C5b. By inhibiting the formation of complement system terminal fragments, Zimura may decrease the activation of inflammasomes and decrease the formation of MAC, thereby potentially avoiding or slowing the degeneration of RPE cells and providing the rationale as a potential therapy for the four conditions that we are targeting. Zimura is a pegylated aptamer, which means that polyethylene glycol is linked to the chemically-synthesized strand of RNA.

Zimura is administered by intravitreal injection. Before a physician administers an intravitreal injection, the patient typically receives topical numbing drops or injection of a numbing agent. In addition, the administering physician typically rinses the ocular surface with an antiseptic solution. By injecting the active agent into the vitreous cavity, the physician delivers the agent in close vicinity to the active disease site with minimal potential for systemic exposure to non-ocular tissues.

An intravitreal injection results in an elevation of intraocular pressure, or IOP, which is usually transient. Labels for the currently approved anti-VEGF agents, which are also administered by intravitreal injection, include descriptions related to monitoring IOP after intravitreal injection of these drugs. In our clinical trials, the IOP is monitored after each intravitreal injection. Based on our clinical experience to date, we have not seen any meaningful or sustained increase in IOP in clinical trials involving multiple intravitreal injections on the same day, and we believe that multiple intravitreal injections likely could be delivered safely in the same day.

We have completed three clinical trials of Zimura to date:

- a Phase 1/2a clinical trial of Zimura monotherapy for the treatment of GA;
- a Phase 1/2a clinical trial of Zimura administered in combination with Lucentis for the treatment of wet AMD; and
- a very small Phase 2a clinical trial of Zimura in combination with anti-VEGF agents for the treatment of IPCV in patients for whom anti-VEGF monotherapy had failed.

Over 100 patients have been treated with Zimura in these three completed trials, with treatment durations extending up to 48 weeks. All doses of Zimura administered in these trials were well-tolerated, with no drug-related safety concerns identified.

Based on our clinical experience with Zimura, the scientific literature around complement in the eye and the positive Phase 2 data outcome for a competitor's C3 complement inhibitor in GA, we believe Zimura holds promise as a potential treatment for several ophthalmic diseases. Our ongoing and planned clinical trials for Zimura, all of which are designed to obtain data to guide potential future development efforts, include the following:

- **OPH2003 (geographic atrophy (GA) secondary to dry AMD)**: an ongoing, randomized, double–masked, sham controlled, multi-center Phase 2b clinical trial evaluating the safety and efficacy of Zimura monotherapy in patients with geographic atrophy, or GA, secondary to dry AMD.
- **OPH2007 (wet AMD)**: an ongoing, randomized dose-ranging, open-label, multi-center Phase 2a clinical trial of Zimura in combination with Lucentis for the treatment of wet AMD in treatment-naïve patients.
- **OPH2006 (IPCV)**: an ongoing, randomized, dose-ranging, open-label Phase 2a clinical trial of Zimura in combination with Eylea for the treatment of IPCV in patients who have not responded to Eylea monotherapy. We are at a very early stage of site initiation and patient recruitment for this trial.
- **OPH2005 (autosomal recessive Stargardt disease (STGD1))**: an ongoing, randomized, double-masked, sham controlled, multi-center Phase 2b clinical trial evaluating the safety and efficacy of Zimura monotherapy for the treatment of autosomal recessive Stargardt disease, referred to as STGD1. We are at a very early stage of patient recruitment for this trial.

- **Non-infectious intermediate and posterior uveitis**: a planned open-label Phase 2a clinical trial of Zimura monotherapy for the treatment of non-infectious intermediate and posterior uveitis, a rare inflammatory disease of the back of the eye.

Our Zimura clinical experience to date, as well as our ongoing and planned clinical trials for Zimura, are described in greater detail below.

Age-related Retinal Disease Clinical Trials

Zimura - Dry AMD Trials

OPH2001: Completed Phase 1/2a Clinical Trial of Zimura for GA Secondary to Dry AMD

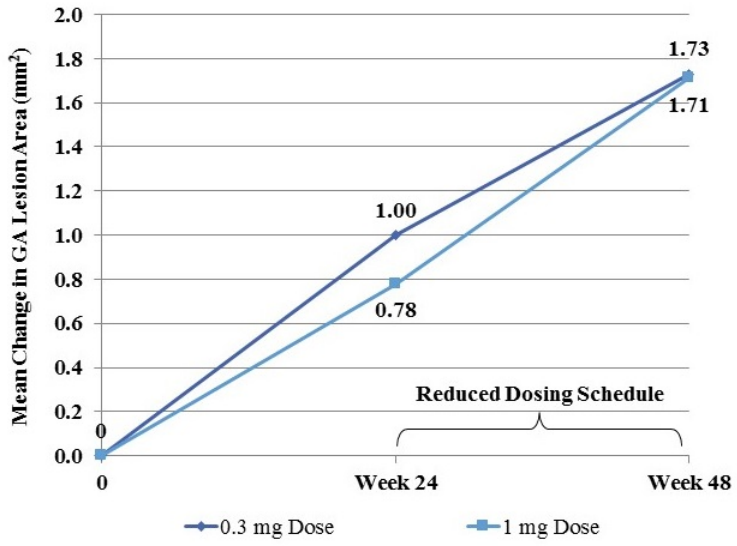
In 2011, we completed a multicenter, uncontrolled, open label Phase 1/2a clinical trial to evaluate the safety and tolerability of Zimura administered as a monotherapy in patients with GA. We enrolled 47 patients in this trial. We randomly assigned patients in this trial to one of two dose groups. Patients received a total of five intravitreal injections of either 0.3 mg or 1 mg of Zimura over a 36-week treatment period. Patients received an intravitreal injection of Zimura at day 0, week 4, week 8, week 24 and week 36 of the trial, with a final follow-up visit at week 48.

Zimura was generally well-tolerated in this trial. We did not observe any evidence of drug related adverse events. We also did not observe any incidence of conversion to wet AMD in eyes treated with Zimura. Adverse events were primarily ocular adverse events in the study eye which were related to the injection procedure.

In addition, we performed assessments of visual acuity to detect any potential decrease in vision associated with intravitreal injections, the administered drug or natural progression of the disease if left untreated. We did not identify any drug related safety issues through measurements of visual acuity.

Our Phase 1/2a clinical trial was an uncontrolled study with a small sample size and was not powered to detect a difference between Zimura dose groups, or the efficacy of Zimura monotherapy, with statistical significance. The primary purpose of the study was to assess safety and tolerability. However, during the more frequent dosing period, we observed a trend, in favor of the higher of two dose groups, of a relative reduction in the mean growth of the GA lesion area, as measured by fundus autofluorescence images read by an independent reading center. Fundus autofluorescence is a common technique for photographing and documenting the size of GA present in the back of the eye, or fundus. Autofluorescence refers to the natural emission of light by biological structures. In fundus autofluorescence images, areas of atrophy are characterized by lower fluorescence.

The mean growth from baseline in the GA lesion area during the first 24 weeks of the trial, when the injections were administered more regularly, was 1.00 mm^2 for the 24 patients receiving the 0.3 mg dose and 0.78 mm^2 for the 23 patients receiving the 1 mg dose. When the injections were administered on a reduced dosing schedule during the subsequent 24 weeks, this relative trend in reduced growth in GA lesion area was no longer present. The following graph sets forth the mean change in GA lesion area from baseline for the two treatment groups over the course of the trial.



We believe this apparent trend in the relative reduction of mean growth in GA lesion area when Zimura was dosed more frequently, together with the relative loss of the benefit when Zimura was dosed less frequently, may suggest a possible drug effect.

OPH2003: Ongoing Phase 2b Trial of Zimura for GA Secondary to Dry AMD

We are currently conducting a randomized, double–masked, sham controlled, multi-center Phase 2b clinical trial evaluating the safety and efficacy of Zimura monotherapy in patients with GA secondary to dry AMD. We initiated this trial during the fourth quarter of 2015. During 2017, based on the announcement of positive data from a competitor studying a different complement inhibitor in a Phase 2 trial in GA, we modified this trial to accelerate the timeline to obtain top-line data. Prior to this initial modification taking effect, we had enrolled approximately 75 patients who were randomized to one of three treatment arms in a 1:1:1 ratio in Part 1 of the trial as follows:

- monthly intravitreal injection of 1 mg of Zimura;
- monthly intravitreal injection of 2 mg of Zimura; and
- monthly sham injection.

Following review of additional third-party clinical trial data and further statistical analysis, we have determined to expand this trial for a total of approximately 275 patients. We are enrolling the approximately 200 remaining patients in Part 2 of the trial by randomizing them to one of three treatment groups in a 1:2:2 ratio as follows:

- monthly intravitreal injection of 2 mg of Zimura plus a sham injection;
- monthly intravitreal injections of 4 mg of Zimura (administered as two injections of 2 mg of Zimura on the same day); and
- monthly sham injections (administered as two separate sham injections).

Patients will be treated for 18 months.

The primary efficacy endpoint is an anatomic endpoint, the mean change in rate of GA growth at 12 months, as measured by fundus autofluorescence. We plan to analyze the primary efficacy endpoint for the 2 mg treatment groups as compared to sham and for the 4 mg treatment group as compared to sham. Given that we have limited data regarding the effect of Zimura in GA, we determined the size of the OPH2003 trial based on our best estimates of the size of trial required to demonstrate a potential clinical benefit for Zimura. This estimate incorporates our assumptions regarding the potential performance of Zimura in this indication based in part on available third-party clinical data and our statistical analysis of this data. Given the information above, this trial could be underpowered to demonstrate a potential clinical benefit for Zimura in this indication.

We submitted to the FDA the amended clinical trial protocol for the initial modification early in the fourth quarter of 2017 and are currently enrolling patients in Part 2 of the trial based on the amended protocol. We plan to further amend the protocol for the increased trial size of 275 patients during the first half of 2018. Based on our anticipated enrollment rate and notwithstanding the protocol amendment to increase the trial size, we expect initial top-line data from this trial to be available during the second half of 2019.

Zimura - Wet AMD Trials

OPH2000: Completed Phase 1/2a Clinical Trial of Zimura for Wet AMD

In 2009, we completed a multicenter, uncontrolled, ascending dose and parallel group, open-label, first in human Phase 1/2a clinical trial to evaluate the safety, tolerability and pharmacokinetic profile of multiple intravitreal injections of Zimura given in combination with multiple doses of 0.5 mg of Lucentis in patients with wet AMD. We enrolled 60 patients in this trial, of which 58 were treatment-naïve patients, and two were treatment-experienced patients.

Patients were treated at one of five Zimura dose levels: 0.03 mg, 0.3 mg, 1 mg, 2 mg and 3 mg. During Part 1 of the trial, a dose-escalation stage, a total of 17 patients were enrolled. Patients received treatment starting at the lowest dose level to be investigated and then further patients were enrolled in a dose-escalation multiple dose scheme in which patients received Zimura dose levels of 0.03 mg, 1 mg, 2 mg or 3 mg. Forty-three patients were subsequently recruited to the second part of the trial, a parallel group stage, in which patients received Zimura dose levels of 0.3 mg, 1 mg, 2 mg or 3 mg. As this was a first in human trial, there were various changes made to the protocol during the trial as data were developed, including a protocol amendment to support a dosing regimen for six monthly injections of Zimura once required toxicology data became available. Seven patients from Part 1 of the study had completed the trial prior to this amendment, and therefore received only three injections of Zimura, while the remaining ten patients from Part 1 received six injections of Zimura. In addition, because of a stability issue with the 3 mg formulation, all patients initially receiving the Zimura 3 mg dose level were switched to the 1 mg dose. The Zimura 2 mg dose level was added to Part 2 of the trial at this time.

Zimura was generally well tolerated in this trial when tested in combination with Lucentis. None of the patients experienced any dose limiting toxicities at any of the dose levels tested. We observed only a single adverse event assessed by the investigators to be related to Zimura, mild subcapsular cataract in one patient in the group treated with 2 mg of Zimura. Despite this event, this patient's visual acuity improved during the study. Adverse events were primarily ocular adverse events in the study eye which were related to the injection procedure. One patient from the 0.3 mg Zimura treatment group withdrew from the trial as a result of a serious adverse event of bacteremia unrelated to study drug or injection procedure, which resulted in a subsequent fatality. Another patient from the 0.3 mg treatment group withdrew from the trial due to investigator's decision. Systemic adverse events in this trial were not frequently reported. No systemic adverse events were assessed as drug related.

Our Phase 1/2a clinical trial was an uncontrolled study with a small sample size and was not powered to detect a difference between Zimura dose groups or the efficacy of Zimura combination therapy with statistical significance. The primary purpose of the study was to assess safety and tolerability. However, in addition to our safety assessment, we performed assessments of visual acuity primarily as safety assessments to detect any decrease in vision associated with the intravitreal drug combination or the injection procedure. We did not identify any safety issues through measurements of visual acuity. There was a general trend towards an improvement in visual acuity seen in all treatment groups. We focused our assessment of vision outcomes on the subgroup of 43 treatment-naïve patients who had received all six Zimura injections at doses of 0.3 mg, 1 mg and 2 mg. This was the most homogeneous group of patients with consistent dosing. We observed a mean increase in visual acuity from baseline at all time points for treatment-naïve patients who received six injections of Zimura at these doses, based on the number of ETDRS letters the patient could read. For this subgroup, at week 24 of the trial, we noted improvements in mean visual acuity from baseline as follows: 13.6 letters for the 13 patients receiving the 0.3 mg dose, 11.7 letters for the 15 patients receiving the 1 mg dose and 15.3 letters for the 15 patients receiving the 2 mg dose. In this subgroup,

22 patients (51%) gained at least 15 ETDRS letters, consisting of six patients (46%) in the 0.3 mg dose group, seven patients (47%) in the 1 mg dose group and nine patients (60%) in the 2 mg dose group.

OPH2004: Phase 2a Trial of Zimura for Treatment-Experienced Wet AMD Patients

During the fourth quarter of 2015, we initiated an open-label Phase 2a clinical trial to evaluate Zimura's potential role when administered in combination with anti-VEGF therapy for the treatment of wet AMD in anti-VEGF treatment-experienced patients who did not respond adequately to anti-VEGF monotherapy. In 2017, following our reassessment of our Zimura development programs, we stopped enrolling patients in this trial as we determined that we would initiate a new Zimura wet AMD trial, the OPH2007 trial described below, for treatment-naïve patients. One patient continues to receive treatment in this trial.

OPH2007: Ongoing Phase 2a Trial of Zimura for Treatment- Naïve Wet AMD Patients

We are currently conducting a randomized, dose-ranging, open-label, multi-center Phase 2a clinical trial of Zimura in combination with 0.5 mg of Lucentis for the treatment of wet AMD. This trial is enrolling treatment-naïve patients. We plan to enroll approximately 60 patients in this trial. We are evaluating different Zimura doses, as well as different combination therapy treatment regimens and dosing intervals in order to obtain information to help guide our potential future development efforts for Zimura in wet AMD.

We plan to evaluate patient data at the 6-month time point. As this is a Phase 2a trial, we plan to evaluate all available safety measures including visual acuity. This trial is an uncontrolled trial with a small sample size designed to assess safety at different dosages and to detect a potential efficacy signal. This trial is not powered to detect a statistically significant difference among the treatment arms or to evaluate the efficacy of Zimura combination therapy with statistical significance.

We initiated this trial during the third quarter of 2017. Based on our anticipated enrollment rate, we expect initial top-line data from this trial to be available by the end of 2018.

Zimura - IPCV Trials

OPH2002: Completed Phase 2a Clinical Trial of Zimura for IPCV

In late 2014, we initiated a very small, uncontrolled, open-label, Phase 2a clinical trial to evaluate Zimura's potential role when administered in combination with anti-VEGF agents for the treatment of IPCV in treatment-experienced patients for whom anti-VEGF monotherapy failed. We enrolled four patients in the trial. None of the patients had a greater than 15-ETDRS letter decrease in visual acuity, which is considered a significant loss in visual acuity, following treatment in this study. There were no findings in relation to ophthalmic examinations which were unexpected or of particular concern.

OPH2006: Ongoing Phase 2a Trial of Zimura for IPCV

We are currently conducting a randomized, dose-ranging, open-label Phase 2a clinical trial of Zimura in combination with Eylea in treatment-experienced patients with IPCV. In this trial, we are enrolling patients who have received three Eylea injections within the previous four months and whose vision has not improved by at least one line on a standard eye chart. We plan to enroll approximately 20 patients in this trial. We are evaluating different Zimura doses, as well as different combination therapy treatment regimens and dosing intervals, in order to obtain information to help guide our potential future development efforts for Zimura in IPCV.

We plan to evaluate patient data at the 9-month time point. As this is a Phase 2a trial, we plan to evaluate all available safety measures including visual acuity. This trial is an uncontrolled trial with a small sample size designed to assess safety at different dosages and to detect a potential efficacy signal. This trial is not powered to detect a statistically significant difference among the treatment arms or to evaluate the efficacy of Zimura combination therapy with statistical significance.

We initiated this trial at the end of 2017 and are currently at a very early stage of site initiation and patient recruitment. Based on our anticipated enrollment rate, we expect initial, top-line data to be available from this trial during the second half of 2019.

Orphan Eye Disease Clinical Trials

Zimura - STDG1 Trial

OPH2005: Ongoing Phase 2b Trial of Zimura for STGD1

We are currently conducting a randomized, double-masked, sham controlled, multi-center Phase 2b clinical trial evaluating the safety and efficacy of Zimura monotherapy for the treatment of STGD1. We plan to enroll approximately 120 patients in this trial, making it one of the largest interventional clinical trials for the treatment of STDG1 to date. Patients are being enrolled as follows:

- approximately 60 patients will be administered:
  - 2 mg of Zimura, followed by 2mg of Zimura 14 days later, monthly for three months during an induction phase; followed by
  - 4 mg of Zimura (administered as two injections of 2 mg of Zimura on the same day), monthly for 15 additional months during a maintenance phase; and
- approximately 60 patients will be administered:
  - a sham injection, followed by a sham injection 14 days later, monthly for three months; followed by
  - two sham injections on the same day, monthly for 15 months.

We plan to evaluate the primary efficacy endpoint at 18-months. The primary efficacy endpoint is an anatomic endpoint, mean rate of change in the area of ellipsoid zone defect, as measured by en-face spectral domain optical coherence tomography, or SD-OCT. SD-OCT is an ultra-high resolution imaging modality commonly used to visualize the retinal tissue. SD-OCT is capable of rendering images in multiple dimensions and from multiple perspectives. This imaging technology allows the demonstration of various layers of the retinal tissue, including the ellipsoid zone, which is rendered in SD-OCT images as a defined layer of photoreceptor cell segments. Areas of defects in the ellipsoid zone can be detected and measured by en-face SD-OCT, which shows an SD-OCT image from the perspective of looking at the retina head on. Scientific literature correlates ellipsoid zone defect with visual dysfunction.

We previously engaged the Foundation Fighting Blindness to provide us with data from the Foundation's publicly available ProgStar study, the largest natural history study on STGD1 disease to date. We have used this natural history data, as well as the perspectives of the key opinion leaders involved in the ProgStar study, as resources to assist in the design of the OPH2005 trial.

We have not previously studied Zimura in STGD1 patients. Given that we have no clinical data regarding the effect of Zimura in STGD1, we determined the size of the OPH2005 trial based on the number of patients with STGD1 that we believe could potentially be enrolled within a reasonable period of time. This number may be increased or decreased in light of the actual enrollment rate during the trial. As STGD1 is an orphan indication, to our knowledge there is only very limited natural history data currently available regarding the variability of the planned primary efficacy endpoint in the STGD1 patient population we plan to enroll in this trial. Given the information above, this trial could be underpowered to demonstrate a potential clinical benefit for Zimura in this indication.

We began enrolling patients in this trial in January 2018 and are currently at a very early stage of patient recruitment. Based on our anticipated enrollment rate, we expect initial top-line data from this trial to be available during 2020.

Zimura - Uveitis Trial

We are currently planning a small, open-label Phase 2a clinical trial of Zimura monotherapy for the treatment of non-infectious intermediate and posterior uveitis, a rare inflammatory disease of the back of the eye. The FDA has recognized non-infections intermediate and posterior uveitis as an orphan disease, with several treatments either approved or in development having received orphan product designation from the FDA. We plan to initiate this trial during 2018. We have not previously studied Zimura in patients with non-infectious intermediate and posterior uveitis.

Gene Therapy Research Programs

As we evaluate the unmet medical need for the treatment of orphan ophthalmic diseases, we have considered that many of these diseases are caused by one or more genetic mutations and currently have no approved treatment options available. Further, the potential to achieve an extended treatment effect and possibly a cure through a single gene therapy administration is particularly appealing to patients who do not have any treatment options, as well as for patients with age-related retinal diseases who currently require chronic therapy over years, if not decades.

Gene therapy consists of delivering DNA encoding for a functional protein to a target tissue to facilitate protein synthesis using a recipient's existing cellular machinery. Gene therapy can be used to replace a non-functional protein produced innately by the subject as a result of a genetic mutation or simply as a means of producing and delivering a therapeutic protein that would not otherwise be produced within the body. The DNA, which is generally delivered by a viral vector, is governed by a promoter sequence which controls transcription of the gene of interest, or transgene, into RNA to initiate protein synthesis. Some of the challenges that gene therapy faces are producing vectors that transfect, or deposit the transgene, in only specific cell types, producing the desired protein at the therapeutic dose levels, and avoiding inducing an inflammatory response that leads to tissue damage. We are particularly interested in adeno-associated virus, or AAV, gene therapy delivery vehicles, as AAV vectors are relatively specific to retinal cells and their safety profile in humans is relatively well-documented as compared to other delivery vehicles and gene therapy technologies currently in development.

In February 2018, we announced that an element of our strategy will include initiating collaborative gene therapy programs focused on discovering and developing novel gene therapy technologies to treat retinal diseases. We intend to investigate promising gene therapy product candidates through collaborations with leading companies and academic and research institutions in the United States and internationally.

For our first gene therapy research collaboration, we have entered into a series of sponsored research agreements with the University of Massachusetts Medical School, or UMMS, and its Horae Gene Therapy Center to utilize their novel gene delivery technologies and "minigene" therapy approach to target retinal diseases. AAV vectors are generally limited as a delivery vehicle by the size of their genetic cargo, which is restricted to approximately 4,700 base pairs of genetic code. The use of "minigenes" as a novel therapeutic strategy seeks to deliver a shortened but still functional form of a larger gene packaged into a standard-size AAV delivery vector. The "minigene" strategy may offer an innovative solution for diseases that would otherwise be difficult to address through conventional AAV gene replacement therapy where the size of the gene of interest exceeds the transgene packaging capacity of conventional AAV vectors. Furthermore, one of the differentiating advantages of the "minigene" approach is that it could potentially provide a treatment that is independent of the specific mutation a patient has. The scope of the UMMS collaboration addresses Leber Congenital Amaurosis type 10, or LCA10, which is the most common type of LCA and is caused by mutations in the CEP290 gene, and STDG1, which is caused by mutations in the ABCA4 gene. LCA10 and STDG1 are both orphan inherited degenerative retinal diseases that lead to vision loss without any FDA or EMA approved treatment. As a condition of each sponsored research agreement, UMMS has granted us an option to obtain an exclusive license to any patents or patent applications that result from the sponsored research.

Remaining Fovista Activities

In December 2016 and August 2017, we received initial top-line data from our three pivotal clinical trials, referred to as OPH1002, OPH1003 and OPH1004, evaluating the anti-platelet derived growth factor, or anti-PDGF, aptamer Fovista® (pegpleranib) administered in combination with anti-VEGF agents for the treatment of wet AMD, indicating that these trials failed to achieve their pre-specified primary endpoints. We have terminated these trials, as well as several other smaller Fovista trials in wet AMD, which we have referred to as the Fovista Expansion Studies. The National Eye Institute and an academic pre-clinical program are evaluating various uses of Fovista for the treatment of retinal capillary hemangiomas associated with the orphan disease Von-Hippel-Lindau Syndrome, and for the treatment of retinoblastoma, a rare cancer of the eye in children, respectively. We have completed our commitments to these two programs, which primarily involved providing Fovista drug product and drug substance that we had on hand for use in the studies.

Therefore, we do not currently expect any development activity for Fovista going forward, as we have no intentions to resume development of Fovista in wet AMD and our supply commitments for the two external studies are complete.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of Zimura or any other product candidate we may develop. Although we rely and intend to continue to rely upon third–party contract manufacturers to produce our products and product candidates, we have recruited personnel with experience to manage

the third–party contract manufacturers we engage to produce Zimura. We do not have any long-term supply arrangements other than as described below.

Zimura is a chemically-synthesized aptamer. In pursuing our business plan, we could acquire or in-license a variety of types of product candidates, including small molecule drugs, protein drugs or biologics, including gene therapies. Small molecule drugs are organic compounds of low molecular weight that are generally associated with ready availability of starting materials and ease of synthesis. In contrast, manufacturing for proteins and biologics is more complex, especially in large quantities. Biologic products must be made consistently and in substantial compliance with a clearly defined manufacturing process, and often must be manufactured under aseptic conditions.

The process for manufacturing Zimura consists of chemical synthesis, pegylation, purification and finally freeze drying to form a powder, which is the active pharmaceutical ingredient, or API. Each of these steps involves a relatively common chemical engineering process. The chemical synthesis is similar to peptide manufacturing. In a separate process that follows the chemical synthesis, API for Zimura is dissolved in a liquid solution that includes certain chemical buffers and then is placed into vials from which the intravitreal injection solution is drawn. This process of rendering the API into a liquid solution and placing it into vials is referred to as fill/finish services.

We currently rely upon a single third-party manufacturer, Agilent Technologies, Inc., or Agilent, to supply us with the chemically synthesized aptamer comprising the API for Zimura and a different, single third-party manufacturer, Ajinomoto Althea, Inc., or Althea, to provide fill/finish services for Zimura. We currently obtain Zimura API from Agilent on a purchase order basis. We have entered into a clinical and commercial services agreement with Althea for fill/finish services for Zimura. This agreement is summarized below. We obtain the polyethylene glycol, or PEG, reagent used to make Zimura from a single third–party manufacturer on a purchase order basis.

Althea Clinical and Commercial Services Agreement

In October 2016, we and Althea entered into a Clinical and Commercial Services Agreement, which we refer to as the Fill/Finish Services Agreement. Pursuant to the Fill/Finish Services Agreement, Althea has agreed to provide clinical and commercial fill/finish services for Zimura as well as any future product candidates that we and Althea may mutually agree. The Fill/Finish Services Agreement has an initial term that will expire at the end of 2027, absent termination by either party in accordance with the terms of the Fill/Finish Services Agreement. The initial term of the Fill/Finish Services Agreement may be extended by mutual agreement of the parties. The amount payable by us to Althea under the Fill/Finish Services Agreement is based on the volume of finished drug product that we order, subject to periodic adjustments over the term of the Fill/Finish Services Agreement. In addition, in the event that we order a specified volume of product, Althea has agreed to supply biological or pharmaceutical drug products meeting certain parameters exclusively to us.

We may cancel any purchase order under the Fill/Finish Services Agreement at any time, subject to the payment of specified cancellation fees. We may terminate the Fill/Finish Services Agreement, without cause, as of any date following the third anniversary of the effective date upon six months' prior notice to Althea. Each party also has the right to terminate the Services Agreement for other customary reasons such as material breach and bankruptcy.

The Fill/Finish Services Agreement contains provisions relating to compliance by Althea with current Good Manufacturing Practices, cooperation by Althea in connection with marketing applications for our product candidates, indemnification, confidentiality, dispute resolution and other customary matters for an agreement of this kind.

Sales and Marketing

We expect that our commercial strategy for any of our product candidates, including whether to retain commercial rights and market and sell the product candidate ourselves or to utilize collaboration, distribution or other marketing arrangements with third parties in some or all geographic markets, will be determined based on a variety of factors, including the size and nature of the patient population, the disease area, the particular indication, the territory in which the product candidate may be marketed and the commercial potential for such product candidate. In addition, our commercial strategy will vary depending on whether the disease is typically treated by general ophthalmology practitioners, specialists, such as retinal specialists, or other sub-specialists. For example, in the United States, retinal specialists perform most of the medical procedures involving diseases of the back of the eye. Intravitreal injection is a specialized procedure. In the vast majority of cases in the United States, retinal specialists perform intravitreal injections. We believe that retinal specialists are sufficiently concentrated that we could effectively promote a product candidate approved for such an indication to these specialists with a targeted specialty sales and marketing group. If successful in the development of any of our product candidates, depending on

the size of the approved indication, we may utilize a variety of types of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize any such product candidate in markets outside the United States.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, generic or biosimilar drug companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of our competitors have significantly greater financial and human resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient enrollment for clinical trials, as well as in acquiring products, product candidates or other technologies that we may target to in-license or acquire in pursuit of our business plan.

Growth of our business through our business plan will be based on our selectively licensing or acquiring and then developing product candidates. Our success will be based in part on our ability to build and actively manage a portfolio of drugs that address or seek to address unmet medical needs and creates value in ophthalmology. However, the acquisition and licensing of pharmaceutical products is a competitive area, and a number of more established companies, which have acknowledged strategies to license and acquire products, may have competitive advantages, as may emerging companies taking similar or different approaches to product acquisition. Established companies pursuing this strategy may have a competitive advantage over us due to their size, cash flows and institutional experience.

The key competitive factors affecting the success of our product candidates, if approved, are likely to be the respective drug's efficacy, safety, method of administration, convenience, price, the level of generic competition and the availability of coverage and reimbursement from government and other third–party payors. The method of administration of Zimura, intravitreal injection, is commonly used to administer ophthalmic drugs for the treatment of sever disease and is generally accepted by patients facing the prospect of sever visual loss or blindness. A therapy that offers a less invasive method of administration, however, might have a competitive advantage over one administered by intravitreal injection, depending on the relative safety of the other method of administration.

We face competition with respect to our product candidates from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies, as well as generic or biosimilar drug companies, worldwide. There are a number of pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of GA, wet AMD, Stargardt disease, non-infectious intermediate and posterior uveitis, or other disease indications for which we may develop Zimura. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. We also will face similar competition with respect to any other products or product candidates that we may seek to develop or commercialize in the future. In particular, many companies are pursuing gene therapy approaches for age-related and orphan retinal diseases.

Competitive considerations for Dry AMD and GA:

- There are a number of products in preclinical research and clinical development by third parties to treat dry AMD, including several that are in development for GA secondary to dry AMD. In general, these product candidates can be categorized based on their proposed mechanisms of action. The mechanisms of action for these product candidates include inflammation suppression, such as complement system inhibitors and corticosteroids, visual cycle modulators, antioxidants and neuroprotectants, cell and gene therapies and vascular perfusion enhancers. Based on publicly available information, we are aware that Novartis AG and MorphoSys AG, Apellis Pharmaceuticals, Inc., Hemera Biosciences, Inc., Achillion Pharmaceuticals, Inc., and Catalyst Biosciences, Inc. each have complement inhibitors in

development for dry AMD, the most advanced of which we believe is Apellis's pegylated, synthetic peptide targeting complement factor C3. Apellis announced positive Phase 2 results for its product candidate and has announced plans to initiate a Phase 3 program during 2018. If Apellis's Phase 3 program for its complement factor C3 product candidate is successful, it is likely that Apellis may obtain marketing approval for its product candidate in advance of when we could reasonably expect marketing approval for Zimura in GA, if at all. Moreover, based on publicly available information, we are aware that several other companies have announced development programs for the treatment of dry AMD targeting different mechanisms of action outside of the complement system.

Competitive considerations for wet AMD:

- There are a number of products in preclinical research and clinical development by third parties to treat wet AMD. Based on publicly available information, we are aware that multiple mechanisms of action are in clinical or pre-clinical development for wet AMD, including Angiopoietin-2 inhibitors, including one in development by Roche, tyrosine kinase inhibitors, integrin inhibitors, novel VEGF inhibitors and complement inhibitors, as well as a few remaining PDGF inhibitors. Within the complement system, we are aware that Apellis is planning a Phase 2 clinical trial with their C3 inhibitor in combination with anti-VEGF therapy. Moreover, based on publicly available information, we are aware that several companies and research organizations are pursuing treatments targeting other molecular targets, potential gene therapy treatments and stem cell transplant treatments for the treatment of wet AMD. In addition, other companies are undertaking efforts to develop technologies to allow for topical dosing of therapeutic agents such as anti-VEGF agents or integrin inhibitors through eye-drops or to allow for a less frequent intravitreal dosing schedule than currently used for standard of care anti-VEGF agents.

- The commercial opportunity for Zimura in wet AMD in particular also could be reduced or eliminated if our competitors develop and commercialize products that reduce or eliminate the use of anti–VEGF drugs for the treatment of patients with wet AMD, since we are only developing Zimura for wet AMD as a combination therapy with anti-VEGF agents. Moreover, we expect that if Zimura is approved for combination therapy for the treatment of wet AMD, the cost of combination treatment would be higher than the cost of treatment of wet AMD with Lucentis, Eylea or particularly Avastin monotherapy. Insurers and other third–party payors may encourage the use of anti–VEGF drugs as monotherapy and discourage the use of Zimura in combination with these drugs. This could limit sales of Zimura for this indication.

Competitive considerations for Stargardt disease:

- There are a number of products in preclinical research and clinical development by third parties to treat Stargardt disease. Based on publicly available information, we are aware that Sanofi, Acucela Inc., Alkeus Pharmaceuticals, Inc., Vision Medicines, Inc., Lin BioScience, Inc., Nightstar Therapeutics plc and ProQR Therapeutics N.V. each have development programs in Stargardt disease. Four of these programs, Acucela, Alkeus, Vision Medicines and Lin BioScience, are exploring the use of oral therapeutics, while Sanofi, with technology provided by Oxford BioMedica plc, and Nightstar are each using a gene therapy approach and ProQR is using an RNA interference approach. Acucela's, Alkeus's and Sanofi's product candidates are each in Phase 2 development.

- In the case of orphan diseases such as Stargardt disease, should we be successful in development, our commercialization efforts may rely on non-patent market exclusivity periods under the Orphan Drug Act of 1983, or the Orphan Drug Act, and the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act. The Orphan Drug Act only provides exclusivity periods for the specific drug granted orphan designation for a specific indication. In addition, there are limited circumstances under each of the Orphan Drug Act and the Hatch-Waxman Act that could result in our loss of data and marketing exclusivity, which could allow a competitor to enter the market. Failure to maintain either data or market exclusivity period would have a material adverse effect on our ability to commercialize our product candidates.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know–how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. We seek to protect our proprietary position, among other methods and where patent protection is available, by filing U.S. and certain foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business, and by maintaining our issued patents. We also rely upon trade secrets, know–how, continuing technological innovation and in–licensing opportunities to develop and maintain our proprietary position.

Our patent portfolio includes the following:

- patents and patent applications in–licensed from Archemix Corp., or Archemix:
    - composition–of–matter patents covering Zimura, which have issued in the United States, the European Union, Japan and certain other jurisdictions, and which are expected to expire in Japan in 2026 and elsewhere in 2025; and composition–of–matter patent applications covering Zimura, which are pending in certain other jurisdictions, and which, if granted, are expected to expire in 2025; and
    - patents covering the treatment of certain complement mediated disorders with Zimura, Zimura for use in a method of treating certain complement mediated disorders or a composition comprising Zimura for treating certain complement mediated disorders, which have issued in the United States, the European Union, Japan and certain other jurisdictions, and which are expected to expire in the United States and Japan in 2026 and elsewhere in 2025; and
- patents and patent applications owned by Ophthotech:
    - patent applications covering co–formulations and other proprietary technology relating to Zimura, which are pending in the United States, the European Union, Japan and certain other jurisdictions, and which, if granted, are expected to expire in 2034.

The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is generally 20 years from the earliest claimed filing date of a non–provisional patent application in the applicable country. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date. The Hatch–Waxman Act permits a patent term extension of up to five years beyond the expiration date of a U.S. patent as partial compensation for the length of time the drug is under regulatory review while the patent is in force. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended.

Similar provisions are available in the European Union and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those products, depending upon the length of the clinical trials for each drug and other factors. The expiration dates referred to above are without regard to potential patent term extension or other market exclusivity that may be available to us.

We may rely, in some circumstances, upon trade secrets to protect our technology. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Licensing Arrangements

We are a party to an agreement with Archemix Corp. or Archemix, under which we in-licensed rights in certain patents, patent applications and other intellectual property related to Zimura. We entered into this agreement to acquire the intellectual property required to develop, manufacture and commercialize Zimura. Our existing in-license for Zimura imposes certain license fee and diligence obligations on us. We expect to enter into acquisition or license agreements in the future, particularly as we pursue our business plan to acquire or in-license additional products, product candidates or other technologies and expand our product pipeline. We expect that any future acquisition or license agreements would impose license fee, royalty payment and diligence obligations on us. In the future, we may also enter into agreements to out-license intellectual property to our collaboration and research partners to assist in the development and, if approved, commercialization of our product candidates. A description of our Zimura license agreement appears below.

Archemix C5 License Agreement

In September 2011, we entered into an amended and restated exclusive license agreement with Archemix relating to anti–C5 aptamers, which we refer to as the C5 agreement. The C5 agreement superseded a July 2007 agreement between us and Archemix. Under the amended and restated agreement, we hold exclusive worldwide licenses (subject to certain pre–existing rights) under specified patents and technology owned or controlled by Archemix to develop, make, use, sell, offer for sale, distribute for sale, import and export pharmaceutical products comprised of or derived from an anti–C5 aptamer for the prevention, treatment, cure or control of human indications, diseases, disorders or conditions of the eye, adnexa of the eye, orbit and optic nerve, other than certain expressly excluded applications.

The license we received under the C5 agreement includes sublicenses to us of rights to specified technology, which we refer to as the SELEX technology, licensed by University License Equity Holdings, Inc., or ULEHI, to Gilead Sciences, Inc., or Gilead, and sublicensed by Gilead to Archemix, as well as sublicenses to us of rights to certain other technology licensed by Gilead to Archemix. The C5 agreement contemplates that our rights to these sublicensed technologies will survive termination of the license from ULEHI to Gilead as long as we are not in breach of the C5 agreement, and will survive termination of the sublicense from Gilead to Archemix as long as such termination did not arise from our action or inaction, provided in each case that we agree to be bound to ULEHI or Gilead, as applicable, under the terms of our agreements with Archemix. However, if Archemix, its affiliates and all of Archemix's assignees and sublicensees, including us, cease to exercise reasonable efforts to develop commercial applications of products and services using the SELEX technology, then Archemix's rights to the SELEX technology may revert to Gilead or ULEHI, and we would lose our rights to the SELEX technology.

Financial Terms

In connection with the C5 agreement, as amended, we paid Archemix an upfront licensing fee of $1.0 million and issued to Archemix an aggregate of 2,000,000 shares of our series A–1 preferred stock and 500,000 shares of our series B–1 preferred stock. We have also paid Archemix an aggregate of $2.0 million in fees based on our achievement of specified clinical milestone events under the C5 agreement.

Under the C5 agreement, for each anti–C5 aptamer product that we may develop under the agreement, including Zimura, we are obligated to make additional payments to Archemix of up to an aggregate of $57.5 million if we achieve specified development, clinical and regulatory milestones, with $30.5 million of such payments relating a first indication, $24.5 million of such payments relating to second and third indications and $2.5 million of such payments relating to sustained delivery applications. Under the C5 agreement, we are also obligated to make additional payments to Archemix of up to an aggregate of $22.5 million if we achieve specified commercial milestones based on net product sales of all anti–C5 products licensed under the agreement. We are also obligated to pay Archemix a double–digit percentage of specified non–royalty payments we may receive from any sublicensee of our rights under the C5 agreement. We are not obligated to pay Archemix a running royalty based on net product sales in connection with the C5 agreement.

Diligence Obligations

We are required to exercise commercially reasonable efforts in developing and commercializing at least one anti–C5 aptamer product and in undertaking investigations and actions required to obtain regulatory approvals necessary to market such product in the United States, the European Union, and Japan, and in such other markets where we determine that it is commercially reasonable to do so.

Term and Termination

Unless earlier terminated, the C5 agreement will expire upon the later of 12 years after the first commercial sale in any country of the last licensed product, the expiration of the last–to–expire valid claim of the licensed patents that covers a licensed product, and the date on which no further payments of sublicensing income are to be received by us.

Either we or Archemix may terminate the C5 agreement if the other party materially breaches the agreement and the breach remains uncured for a specified period. Archemix may also terminate the C5 agreement, or may convert our exclusive license under the agreement to a non–exclusive license, if we challenge or assist a third party in challenging the validity or enforceability of any of the patents licensed under the agreement. We may terminate the agreement at any time and for any or no reason effective at the end of a specified period following our written notice of termination to Archemix.

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, pricing, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post–approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs and Biologics in the United States

In the United States, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. Biologic products, including gene therapy products, are licensed for marketing under the Public Health Service Act, or PHSA. The failure to comply with requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities, including state agencies.

A drug candidate must be approved by the FDA through a new drug application, or NDA. A biologic candidate is licensed by FDA through approval of a biologic license application, or BLA. An applicant seeking approval to market and distribute a new product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an investigational new drug application, or IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well–controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication and the safety, potency and purity of a candidate biologic product for each indication;
- preparation and submission to the FDA of an application requesting marketing for one or more proposed indications;
- review by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or

cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;

- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the application; and
- compliance with any post–approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post–approval studies.

Preclinical Studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, and the purity and stability of the substance, as well as *in vitro* and animal studies to assess the potential safety and activity of the product candidate for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved product to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational product to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved application. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30–day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30–day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee, or DSMB. This group provides authorization as to whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Human Clinical Trials in Support of an Application

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in four sequential phases, which may overlap or be combined:

- ***Phase 1.*** The product candidate is initially introduced into a small number of healthy human subjects or, in certain indications, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

- ***Phase 2.*** The product candidate is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage. Phase 2a clinical trials tend to be smaller pilot studies for the purpose of demonstrating biological activity and clinical "proof of concept." Phase 2b studies tend to be larger studies focused on finding the optimal dosage and may be controlled.

- ***Phase 3.*** These clinical trials are commonly referred to as “pivotal” studies, which denotes a study that presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a product candidate. The product candidate is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well–controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, identify adverse effects, establish the overall risk–benefit profile of the product and to provide adequate information for the labeling of the product.

- ***Phase 4.*** Post–approval studies may be required to be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the safety results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product candidate; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA or the sponsor or the data monitoring committee may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Special Regulations and Guidance Governing Gene Therapy Products

The FDA has defined a gene therapy product as one that mediates its effects by transcription and/or translation of transferred genetic material and/or by integrating into the host genome and which is administered as nucleic acids, viruses, or genetically engineered microorganisms. The products may be used to modify cells *in vivo* or transferred to cells *ex vivo* prior to administration to the recipient. Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. Within CBER, the review of gene therapy and related products is consolidated in the Office of Cellular, Tissue and Gene Therapies, and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews. CBER works closely with the NIH and the Recombinant DNA Advisory Committee, or RAC, a federal advisory committee, which makes recommendations to the NIH on gene therapy issues and engages in a public discussion of scientific, safety, ethical, and societal issues related to proposed and ongoing gene therapy protocols. The FDA and the NIH have published guidance documents with respect to the development and submission of gene therapy protocols.

In addition to the foregoing, products classified as gene therapies are subject to additional regulation. The FDA has issued various guidance documents regarding gene therapies. Although the FDA has indicated that these guidance documents are not legally binding, we believe that our compliance with them is likely necessary to gain approval for any product candidate we may develop. The guidance documents provide additional factors that the FDA will consider at each of the above stages of development and relate to, among other things, the proper preclinical assessment of gene therapies; the chemistry, manufacturing, and control information that should be included in an IND application; the proper design of tests to measure product potency in support of an IND or BLA application; and measures to observe delayed adverse effects in subjects who have been exposed to investigational gene therapies when the risk of such effects is high. Further, the FDA usually recommends that sponsors observe subjects for potential gene therapy–related delayed adverse events for a 15–year period, including a minimum of five years of annual examinations followed by 10 years of annual queries, either in person or by questionnaire.

If a gene therapy trial is conducted at, or sponsored by, institutions receiving the NIH funding for recombinant DNA research, a protocol and related documentation must be submitted to, and the study registered with, the NIH Office of Biotechnology Activities, or OBA, pursuant to the NIH Guidelines for Research Involving Recombinant DNA Molecules prior

to the submission of an IND to the FDA. In addition, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. The NIH will convene the RAC to discuss protocols that raise novel or particularly important scientific, safety or ethical considerations at one of its quarterly public meetings. The OBA will notify the FDA of the RAC's decision regarding the necessity for full public review of a gene therapy protocol. RAC proceedings and reports are posted to the OBA web site and may be accessed by the public.

Further, to facilitate adverse event reporting and dissemination of additional information about gene therapy trials, the FDA and the NIH established the Genetic Modification Clinical Research Information System, or GeMCRIS. Investigators and sponsors of a human gene transfer trials can utilize this web–based system to report serious adverse events and annual reports. GeMCRIS also allows members of the public to access basic reports about human gene transfer trials registered with the NIH and to search for information such as trial location, the names of investigators conducting trials, and the names of gene transfer products being studied.

Finally, for a gene therapy product, the FDA also will not approve the product if the manufacturer is not in compliance with good tissue practices, or GTP. These standards are found in FDA regulations and guidances that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues, and cellular and tissue based products, or HCT/Ps, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the GTP requirements is to ensure that cell and tissue based products are manufactured in a manner designed to prevent the introduction, transmission, and spread of communicable disease. FDA regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through screening and testing.

Review of a Candidate Product by the FDA

If clinical trials are successful, the next step in the development process is the preparation and submission to the FDA of an application. The application is the vehicle through which applicants formally propose that the FDA approve a new drug for marketing and sale in the United States for one or more indications. The application must contain a description of the manufacturing process and quality control methods, as well as results of preclinical tests, toxicology studies, clinical trials and proposed labeling, among other things. Every new product must be the subject of an approved application before it may be commercialized in the United States. Under federal law, the submission of most applications is subject to an application user fee, which for federal fiscal year 2018 is $2,421,495 for an application requiring clinical data. The sponsor of an approved application is also subject to an annual program fee, which for fiscal year 2018 is $304,162. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

Following submission of an application, the FDA conducts a preliminary review of an application generally within 60 calendar days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an application for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in–depth substantive review. Under the Prescription Drug User Fee Act, or PDUFA, the FDA has agreed to specified performance goals in the review process of applications. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the application for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of drugs that are not NMEs, the ten–month and six–month review periods run from the date that FDA receives the application. The review process and the PDUFA goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured, stored, packaged and tested. These pre–approval inspections may cover all facilities associated with an application submission, including component manufacturing (e.g., active pharmaceutical ingredients), finished product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an application, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Under the FDA Reauthorization Act of 2017, the FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain applications, including applications for products in shortage or those for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is an NME.

The FDA is required to refer an application for a novel product candidate to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA's Decision on an Application

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the application, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post–approval studies, including Phase 4 clinical trials, be conducted to further assess the product candidate's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post–market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations and Accelerated Approval

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life–threatening disease or condition. These programs are fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation. The FDA may also approve certain products based on an accelerated basis.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life–threatening disease or condition, and if the product demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the application is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

In 2012, Congress enacted the Food and Product Administration Safety and Innovation Act, or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life–threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to

breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross–disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

The FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case– by–case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment–limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

With passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Finally, the FDA may grant accelerated approval to a product for a serious or life–threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

Post–Approval Requirements

Products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, manufacturers and other entities involved in the manufacture and distribution of approved products are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third–party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information;

imposition of post–market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post–approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off–label uses, and a company that is found to have improperly promoted off–label uses may be subject to significant liability.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch–Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are “abbreviated” because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference–listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is “bioequivalent” to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if “the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug...” Upon approval of an ANDA, the FDA indicates whether the generic product is “therapeutically equivalent” to the RLD in its publication “Approved Drug Products with Therapeutic Equivalence Evaluations,” also referred to as the “Orange Book.” Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA’s designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch–Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non–patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non–patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety, which is the molecule or ion responsible for the action of the drug substance, that has previously been approved by the FDA in any other NDA. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight (8) months for a drug that has three (3) or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes FDA to expedite review of ‘‘competitor generic therapies’’ or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

505(b)(2) NDAs

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA pursuant to an NDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch–Waxman Amendments and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant. If the 505(b)(2) applicant can establish that reliance on FDA's previous findings of safety and effectiveness is scientifically and legally appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements, including clinical trials, to support the change from the previously approved RLD. The FDA may then approve the new product candidate for all, or some, of the label indications for which the RLD has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

Hatch–Waxman Patent Certification and the 30–Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA or 505(b)(2) applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the RLD in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved RLD's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the applicant is not seeking approval).

If the ANDA or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA or the 505(b)(2) application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) application until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the applicant. The ANDA or 505(b)(2) application also will not be approved until any applicable non–patent exclusivity listed in the Orange Book for the branded reference drug has expired.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of an NCE, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Biosimilars and Exclusivity

The 2010 Patient Protection and Affordable Care Act, which was signed into law on March 23, 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009 or BPCIA. That Act established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. As of January 1, 2018, the FDA has approved nine biosimilar products for use in the United States. No interchangeable biosimilars have been approved. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Additional guidances are expected to be finalized by FDA in the near term.

Under the Act, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

Patent Term Restoration and Extension

A patent claiming a new drug product or its method of use may be eligible for a limited patent term extension, also known as patent term restoration, under the Hatch–Waxman Amendments, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. Patent term extension is generally available only for drug products whose active ingredient has not previously been approved by the FDA. The restoration period granted is typically one–half the time between the effective date of an IND and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term extension cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an

approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The United States Patent and Trademark Office (PTO) reviews and approves the application for any patent term extension in consultation with the FDA.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act, an application or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the FDASIA in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and any other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

For drugs intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, FDA will meet early in the development process to discuss pediatric study plans with sponsors and FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety (90) days after FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless and until FDA promulgates a regulation stating otherwise, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity or patent protection, including the non–patent and orphan exclusivity. This six–month exclusivity may be granted if an application sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. With regard to patents, the six–month pediatric exclusivity period will not attach to any patents for which an ANDA or 505(b)(2) applicant submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by the proposed product.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an application for the product and rare disease or condition. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same product for the same indication for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different indications. If a product designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same product for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

The 21st Century Cures Act

On December 13, 2016, President Barack H. Obama signed the 21st Century Cures Act, or Cures Act, into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increasing funding for the FDA to spend on innovation projects. The new law also amends the PHSA to reauthorize and expand funding for the NIH. The Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges the NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the PHSA, Title III of the Cures Act seeks to accelerate the discovery, development, and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes the existing priority review voucher program for certain products intended to treat rare pediatric diseases until 2020; creates a new priority review voucher program for product applications determined to be material national security threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires the FDA to evaluate the potential use of “real world evidence” to help support approval of new indications for approved products; provides a new “limited population” approval pathway for antibiotic and antifungal products intended to treat serious or life-threatening infections; and authorizes the FDA to designate a product as a “regenerative advanced therapy,” thereby making it eligible for certain expedited review and approval designations.

Review and Approval of Products in Europe and other Foreign Jurisdictions

In addition to regulations in the United States, a manufacturer is subject to a variety of regulations in foreign jurisdictions to the extent it chooses to sell any products in those foreign countries. Even if a manufacturer obtains FDA approval of a product, it must still obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. To obtain regulatory approval of an investigational product in the European Union, a manufacturer must submit a marketing authorization application, or MAA, to the European Medicines Agency, or EMA. For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, clinical trials are to be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Clinical Trial Approval in the European Union

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on Good Clinical Practice, an applicant must obtain approval from the competent national authority of the European Union Member State, or the EU Member State, in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion.

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation will be directly applicable to and binding in all EU Member States without the need for any national implementing legislation. The new Clinical Trials Regulation (EU) No 536/2014 was published on June 16, 2014 but is not expected to apply until 2019. The conduct of all clinical trials performed in the European Union will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. It will overhaul the current system of approvals for clinical trials in the European Union. Specifically, the new legislation aims at simplifying and streamlining the approval of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU Member State (RMS) through an EU Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single EU Member State or in more than one EU Member State. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials.

PRIME Designation in the EU

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the Committee for Human Medicinal Products, or CHMP, or Committee for Advanced Therapies, or CAT, are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Marketing Authorization

In the European Union, marketing authorizations for medicinal products may be obtained through several different procedures founded on the same basic regulatory process.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid across the European Economic Area (i.e. the European Union as well as Iceland, Liechtenstein and Norway). The centralized procedure is compulsory for medicinal products produced by certain biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for the treatment of certain diseases. It is optional for those products that are highly innovative or for which a centralized process is in the interest of patients. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Accelerated evaluation may be granted by the CHMP in exceptional cases. These are defined as circumstances in which a medicinal product is expected to be of a "major public health interest." Three cumulative criteria must be fulfilled in such circumstances: the seriousness of the disease, such as severely disabling or life–threatening diseases, to be treated; the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In these circumstances, the EMA ensures that the opinion of the CHMP is given within 150 days.

Specifically, the grant of marketing authorization in the European Union for products containing viable human tissues or cells such as gene therapy medicinal products is governed by Regulation 1394/2007/EC on advanced therapy medicinal products, read in combination with Directive 2001/83/EC of the European Parliament and of the Council, commonly known as the Community code on medicinal products. Regulation 1394/2007/EC lays down specific rules concerning the authorization, supervision, and pharmacovigilance of gene therapy medicinal products, somatic cell therapy medicinal products, and tissue engineered products. Manufacturers of advanced therapy medicinal products must demonstrate the quality, safety, and efficacy of their products to EMA which provides an opinion regarding the application for marketing authorization. The European Commission grants or refuses marketing authorization in light of the opinion delivered by EMA.

The decentralized procedure provides for approval by one or more other concerned EU Member States of an assessment of an application for marketing authorization conducted by one EU Member State, known as the reference EU Member State. In accordance with this procedure, an applicant submits an application for marketing authorization to the reference EU Member State and the concerned EU Member States. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States which, within 90 days of receipt, must decide whether to approve the assessment report and related materials.

If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU Member States. In accordance with the mutual recognition procedure, the sponsor applies for national marketing authorization in one EU Member State. Upon receipt of this authorization the sponsor can then seek the recognition of this authorization by other EU Member States. Authorization in accordance with either of these procedures will result in authorization of the medicinal product only in the reference EU Member State and in the other concerned EU Member States.

A marketing authorization may be granted only to an applicant established in the European Union. Regulation No. 1901/2006 provides that, prior to obtaining a marketing authorization in the European Union, an applicant must demonstrate compliance with all measures included in a Pediatric Investigation Plan, or PIP, approved by the Pediatric Committee of the EMA, covering all subsets of the pediatric population, unless the EMA has granted a product–specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP.

Regulatory Data Exclusivity in the European Union

In the European Union, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance the centralized authorization procedure. Data exclusivity prevents applicants for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals in the European Union

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk–benefit balance by the EMA or by the competent authority of the relevant EU Member State. To that end, the marketing authorization holder must provide the EMA or the relevant competent authority of the EU Member State with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the relevant competent authority of the EU Member State decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five–year renewal period. Any marketing authorization that is not followed by the marketing of the medicinal product on the EU market (in the case of the centralized procedure) or on the market of the EU Member State which delivered the marketing authorization within three years after authorization ceases to be valid.

Regulatory Requirements after Marketing Authorization

As in the United States, marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU Member States both before and after grant of the manufacturing and marketing authorizations.

The holder of an EU marketing authorization for a medicinal product must also comply with EU pharmacovigilance legislation and its related regulations and guidelines, which detail requirements for conducting pharmacovigilance or the assessment and monitoring of the safety of medicinal products. These rules can impose on central marketing authorization holders for medicinal products the obligation to conduct a labor intensive collection of data regarding the risks and benefits of marketed products and to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies.

The manufacturing process for medicinal products in the European Union is highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the European Union with the intention to import the active pharmaceutical ingredients into the European Union. Similarly, the distribution of medicinal products into and within the European Union is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU Member States.

In the European Union, the advertising and promotion of products are subject to EU Member States' laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU Member States may apply to the advertising and promotion of

medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off–label promotion. The off–label promotion of medicinal products is prohibited in the European Union. The applicable laws at the European Union level and in the individual EU Member States also prohibit the direct–to–consumer advertising of prescription–only medicinal products. These laws may further limit or restrict the advertising and promotion of products to the general public and may also impose limitations on promotional activities with health care professionals.

Pediatric Studies and Exclusivity

Prior to obtaining a marketing authorization in the European Union, applicants must demonstrate compliance with all measures included in an EMA–approved PIP covering all subsets of the pediatric population, unless the EMA has granted a product–specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are laid down in Regulation (EC) No 1901/2006, the so–called Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine for children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine for children is not needed or is not appropriate, such as for diseases that only affect the elderly population. Before an MAA can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP. If an applicant obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the Centralized Procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate, or SPC.

Orphan Drug Designation and Exclusivity in the European Union

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that the product is intended for the diagnosis, prevention or treatment of: (1) a life–threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Union when the application is made, or (2) a life–threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives the medicinal product is unlikely to be developed. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States and, in addition, a range of other benefits during the development and regulatory review process, including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if the product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union (commonly referred to as "Brexit"). Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the United Kingdom from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to the EU Treaty. Since the regulatory framework for pharmaceutical products in the United Kingdom, covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products, is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in

the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third–party payors to reimburse all or part of the associated healthcare costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third–party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third–party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost–effectiveness of medical products and services and imposing controls to manage costs. Third–party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost–effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third–party payor not to cover a product candidate could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost–containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Government authorities and third–party payors, particularly Medicare, have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications and encouraging the substitution of lower cost or generic products. Pricing pressures recently experienced by the pharmaceutical industry may be further exacerbated by legislative and policy changes under consideration by the Trump Administration. For example, the new administration has expressed an interest in authorizing and/or directing the Center for Medicare & Medicaid Service or other agencies of the U.S. government to negotiate prices for products covered by Medicare directly with pharmaceutical companies. If this were to occur, especially for wet AMD products, where a large portion of the patient population is elderly and is therefore covered by Medicare, there could be significant downward pressure on prices charged, not only for patients covered by Medicare, but also for patients covered by private insurers who may follow the government's lead on price. Adoption of price controls and cost–containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third–party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require a clinical trial that compares the cost effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost–effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the

profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade, i.e., arbitrage between low–priced and high–priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third–party payors play a primary role in the recommendation and prescription of products that are granted marketing approval. Arrangements with providers, consultants, third–party payors and customers are subject to broadly applicable fraud and abuse, anti–kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti–Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or collectively the ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws and regulations, such as state anti–kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non–governmental third–party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pharmaceutical Insurance Coverage and Health Care Reform

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the United States. In March 2010, the ACA was enacted, which includes measures that have significantly changed health care financing by both governmental and private insurers. The provisions of the ACA of importance to the pharmaceutical and biotechnology industry are, among others, the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drug agents or biologic agents, which is apportioned among these entities according to their market share in certain government health care programs;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, unless the drug is subject to discounts under the 340B drug discount program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements under the federal Physician Payments Sunshine Act for manufacturers to report information related to payments and other transfers of value made to physicians and teaching hospitals as well as ownership or investment interests held by physicians and their immediate family members;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- creation of the Independent Payment Advisory Board, which, if and when impaneled, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription products; and
- establishment of a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription product spending.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and will stay in effect through 2024 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to

five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of products under Medicare and reform government program reimbursement methodologies for products.

These healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price for any approved product and/or the level of reimbursement physicians receive for administering any approved product. Reductions in reimbursement levels may negatively impact the prices or the frequency with which products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Since enactment of the ACA, there have been numerous legal challenges and congressional actions to repeal and replace provisions of the law. In May 2017, the U.S. House of Representatives passed legislation known as the American Health Care Act of 2017. Thereafter, the Senate Republicans introduced and then updated a bill to replace the ACA known as the Better Care Reconciliation Act of 2017. The Senate Republicans also introduced legislation to repeal the ACA without companion legislation to replace it, and a “skinny” version of the Better Care Reconciliation Act of 2017. In addition, the Senate considered proposed healthcare reform legislation known as the Graham-Cassidy bill. None of these measures was passed by the U.S. Senate.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 2017, President Donald J. Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Administration announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

More recently, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Congress will likely consider other legislation to replace elements of the ACA, during the next congressional session.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of products under Medicare and reform government program reimbursement methodologies for products. At the federal level, Congress and the Trump Administration have each indicated that it will continue to seek new legislative and/or administrative measures to control costs. At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription product and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

Employees

As of January 31, 2018, we had 38 full–time employees, including a total of 3 employees with M.D. or Ph.D. degrees. Of our workforce, 17 employees are engaged in research and development. During the year ended December 31, 2017, the

Company's workforce was reduced by approximately 122 employees in connection with a reduction in personnel announced in December 2016 and natural attrition. None of our employees are represented by labor unions or covered by collective bargaining agreements.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in 2007. Our principal executive offices are located at One Penn Plaza, 35th Floor, New York, NY 10119, and our telephone number is (212) 845–8200. Our Internet website is http://www.ophthotech.com.

Available Information

We make available free of charge through our website our Annual Report on Form 10–K, Quarterly Reports on Form 10–Q, Current Reports on Form 8–K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. You can find, copy and inspect information we file at the SEC's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. Please call the SEC at 1–800–SEC–0330 for more information about the operation of the SEC's public reference room. You can review our electronically filed reports and other information that we file with the SEC on the SEC's web site at http://www.sec.gov. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. The information contained on, or that can be accessed through, our website is not a part of or incorporated by reference in this Annual Report on Form 10–K.

Item 1A. Risk Factors.

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 1 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Business Plan, Financial Position and Need for Additional Capital

We are in the process of implementing a business plan that may continue to evolve as we await relevant clinical data and evaluate new opportunities. Our business plan may lead to the initiation of one or more development programs or the execution of one or more transactions that you do not agree with or that you do not perceive as favorable to your investment.

In early 2017, we began a process to review our strategic alternatives, including identifying potential business development opportunities. Also beginning in early 2017, we undertook a reassessment of our development plans for Zimura and Fovista, which included an evaluation of the scientific rationale for potentially developing these product candidates in one or more other ophthalmic indications for which there is a high unmet need.

In July 2017, we announced that we are pursuing a strategy to leverage our clinical experience and retina expertise to identify and develop therapies to treat multiple ophthalmic orphan diseases for which there are limited or no treatment options available. In parallel, we also determined that we would continue our Zimura programs in age-related retinal diseases. In February 2018, we announced that an element of our strategy will include initiating gene therapy collaborations focused on discovering and developing novel gene therapy technologies to treat retinal diseases. We intend to investigate promising gene therapy product candidates through collaborations with leading companies and academic and research institutions in the United States and internationally. We continue to be actively engaged in extensive business development efforts to identify, evaluate and potentially obtain rights to and develop additional therapeutic and gene therapy product candidates that would complement our strategic goals and leverage our competitive advantages.

This business plan requires us to be successful in a number of challenging, uncertain and risky activities, including pursuing development of Zimura in indications for which we have limited or no human clinical data, identifying promising new assets for development that are available for acquisition or in-license and that fit our strategic focus and, if so identified,

negotiating and executing an acquisition or in-license agreement for one or more of those programs on favorable terms, converting early stage gene therapy research efforts into clinical development opportunities, building internal or outsourced gene therapy capabilities and designing and executing a pre-clinical and/or clinical development program for any newly acquired product candidates. We may not be successful at one or more of the activities required for us to execute this business plan. We are also continuing to consider other alternatives, including mergers or other transactions involving our company as a whole or other collaboration transactions. We cannot be sure when or if this process will result in any type of transaction. Even if we pursue a transaction, such transaction may not be consistent with our stockholders' expectations or may not ultimately be favorable for our stockholders, either in the shorter or longer term.

Our growth prospects and the future value of our company are primarily dependent on the progress of our ongoing and planned clinical development programs for Zimura and the outcome of our ongoing business development efforts and pipeline expansion activities, together with the amount of our remaining available cash. The development of Zimura and the outcome of our ongoing business development efforts and pipeline expansion activities are highly uncertain.

We have only very limited data from small, uncontrolled clinical trials regarding the safety and efficacy of Zimura as a monotherapy for the treatment of GA or in combination with anti-VEGF agents for the treatment of wet AMD or IPCV, and we have no human clinical data regarding the safety and efficacy of Zimura as a treatment for autosomal recessive Stargardt disease, referred to as STGD1, or non-infectious intermediate and posterior uveitis. Our prior Zimura trials were not powered to demonstrate the efficacy of Zimura therapy with statistical significance. We determined the size of the OPH2003 trial in GA based on our best estimates of the size of trial required to demonstrate a potential clinical benefit for Zimura. This estimate incorporates our assumptions regarding the potential performance of Zimura in this indication based in part on available third-party clinical data and our statistical analysis of this data. In addition, we determined the size of the OPH2005 trial in STDG1 based on the number of patients with STGD1 that we believe could potentially be enrolled within a reasonable period of time. This number may be increased or decreased in light of the actual enrollment rate during the trial. As STGD1 is an orphan indication, to our knowledge there is only very limited natural history data currently available regarding the variability for our planned primary efficacy endpoint in the STGD1 patient population we plan to enroll in this trial. Given the information above, these trials could be underpowered to demonstrate a potential clinical benefit for Zimura in these indications.

With respect to business development efforts and pipeline expansion activities, our research collaboration with UMMS is for very early stage technology which may never translate into clinical development programs. We may be unable to secure additional collaborations, partnerships or in-licensing or acquisition opportunities.

We may continue to reassess and make changes to our existing development programs and pipeline expansion strategy. Our future plans for our Zimura development program may be affected by the results of competitors' clinical trials of complement inhibitors. Our plans for our business development efforts and pipeline expansion activities may be affected by the results of competitors' ongoing research and development efforts. We may modify, expand or terminate some or all of our development programs, clinical trials or collaborative research programs at any time as a result of new competitive information or as the result of changes to our product pipeline or business development strategy.

We expect that our remaining cash balances will continue to decline as we pursue these development programs, pursue our collaborative research programs, pursue our business development activities and until such time, if any, as we receive additional funding, and the value of our stockholders' investment may decline as a result.

Our strategy of obtaining rights to products, product candidates or technologies for the treatment of ophthalmic diseases through in-licenses and acquisitions may not be successful. Our failure to successfully expand our clinical pipeline would likely impair our ability to grow.

An important element of our strategy has been and continues to be to expand our product pipeline through potentially in-licensing or acquiring the rights to products, product candidates or technologies that would complement our strategic goals as well as other compelling ophthalmology opportunities. In addition, we have recently added gene therapy research as an area of interest for our strategy. Because we expect generally that we will not engage directly in internal early stage research and drug discovery efforts, the future growth of our business beyond our current product portfolio will depend significantly on our ability to in-license or acquire the rights to approved products, additional product candidates or technologies, including any promising product candidates that may emerge from our collaborative gene therapy research programs, including, for example, our collaboration with UMMS, for which we have an option to obtain an exclusive license to patents and patent applications resulting from the sponsored research but for which we have not yet agreed to license terms. We may be unable, however, to in-license or acquire the rights to any such products, product candidates or technologies from third parties for several reasons. The success of this strategy depends partly upon our ability to identify, select and acquire or in-license promising product candidates

and technologies. We may be unable to identify suitable products, product candidates or technologies within our area of focus. The process of proposing, negotiating and implementing a license or acquisition of a product candidate is lengthy and complex.

The in-licensing and acquisition of pharmaceutical products is an area characterized by intense competition, and a number of companies (both more established and early stage biotechnology companies) are also pursuing strategies to in-license or acquire products, product candidates or technologies that we may consider attractive. We believe that other companies may be particularly active in pursuing opportunities to in-license or acquire promising gene therapy opportunities. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities, while earlier stage companies may be more aggressive or have a higher risk tolerance. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to in-license or acquire the rights to the relevant product, product candidate or technology on terms that would allow us to make an appropriate return on our investment. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts or we may incorrectly judge the value or worth of an acquired or in-licensed product candidate or technology.

Further, any product candidate that we acquire would most likely require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate would not be shown to be sufficiently safe and effective for approval by regulatory authorities.

If we are unable to successfully obtain rights to suitable products, product candidates or technologies, our business, financial condition and prospects for growth could suffer. In addition, acquisitions and in-licensing arrangements for product candidates and technologies are inherently risky, and ultimately, if we do not complete an announced acquisition or license transaction or integrate an acquired or licensed product or technology successfully and in a timely manner, we may not realize the benefits of the acquisition or license to the extent anticipated and the perception of the effectiveness of our management team and our company may suffer in the marketplace. In addition, even if we are able to successfully identify, negotiate and execute one or more transactions to acquire or in-license new products, product candidates or technologies, our expenses and short-term costs may increase materially and adversely affect our liquidity.

In addition, future acquisitions and in-licenses may entail numerous operational, financial and legal risks, including:

- exposure to known and unknown liabilities, including possible intellectual property infringement claims, violations of laws, tax liabilities and commercial disputes;
- incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;
- higher than expected acquisition and integration costs;
- difficulty in combining the operations and personnel of any acquired businesses with our operations and personnel;
- inability to maintain uniform standards, controls, procedures and policies;
- restructuring charges related to eliminating redundancies or disposing of assets as part of any such combination;
- large write-offs and difficulties in assessing the relative percentages of in-process research and development expense that can be immediately written off as compare to the amount that must be amortized over the appropriate life of the asset;
- increased amortization expenses or, in the event that we write-down the value of acquired assets, impairment losses;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership;
- inability to retain personnel, key customers, distributors, vendors and other business partners integral to an in-licensed or acquired product candidate or technology;

- potential failure of the due diligence processes to identify significant problems, liabilities or other shortcomings or challenges of an acquired or licensed product candidate or technology, including, without limitation, problems, liabilities or other shortcomings or challenges with respect to intellectual property, product quality, revenue recognition or other accounting practices, partner disputes or issues and other legal and financial contingencies and known and unknown liabilities; and

- entry into therapeutic modalities, indications or markets in which we have no or limited direct prior development or commercial experience and where competitors in such markets have stronger market positions.

If we are unable to successfully manage our acquisitions or other in-license transactions, our ability to develop new products and continue to expand and diversify our product pipeline may be limited.

We may not use our available cash and other sources of funding effectively as we pursue our business plan.

Our business plan may not be successful, or we may be unsuccessful in effectively executing our business plan, which, in either case, could result in the expenditure of our available cash and other sources of funding in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our available cash in a manner that does not produce adequate income, if any, or that loses value. For example, as we implement our revised business plan, we could allocate our available capital resources to pursue the development or acquisition of a particular product candidate or technology that proves to be ineffective, or we could fail to allocate sufficient resources to strategic opportunities or product candidates or technologies that may be more profitable or for which there is a greater likelihood of success. If we fail to effectively allocate our available capital resources, we may not be able to achieve our goals, and our financial condition and prospects for growth could suffer.

Our limited operating history may make it difficult for our stockholders to evaluate the success of our business to date and to assess our future viability.

We were incorporated and commenced active operations in 2007. Our operations to date have been focused on organizing and staffing our company, acquiring rights to product candidates, business planning, raising capital and developing Zimura, Fovista and other product candidates. We have not yet demonstrated our ability to successfully complete a large-scale, pivotal clinical trial with safety and efficacy data sufficient to obtain marketing approval, apply for and obtain marketing approval, qualify a commercial manufacturer through a pre-approval inspection with respect to any of our products, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. The failure of our pivotal Phase 3 program for Fovista for the treatment of wet AMD has required us to reevaluate our future development plans for our product candidates, as well as our business plan more broadly, and has significantly decreased the likelihood that we will have a commercial product in the near term. We may never be successful in developing or commercializing any of our product candidates. If successful in developing and obtaining marketing approval of one of our product candidates, we would need to transition from a company with a product development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We have a history of significant operating losses. We expect to continue to incur losses until such time, if ever, that we successfully commercialize our product candidates and may never achieve or maintain profitability.

Since inception, we have experienced significant cash outflows in funding our operations. To date, we have not generated any revenues from product sales and have financed our operations primarily through private placements of our preferred stock, venture debt borrowings, funds received under our royalty purchase and sale agreement with Novo A/S, which we refer to as the Novo Agreement, which we entered into in May 2013, our initial public offering, which we closed in September 2013, our follow-on public offering, which we closed in February 2014, and funds we received under the Fovista Licensing and Commercialization Agreement with Novartis Pharma, AG, which we refer to as the Novartis Agreement, which we entered into in May 2014. As of December 31, 2017, we had an accumulated deficit of $484.8 million. Although we had net income of $114.2 million for the year ended December 31, 2017, all of the revenue associated with such net income was on account of the recognition during the period, especially during the third quarter of 2017, of revenue under the relative selling price method that related to the consideration that we had received in prior periods under the Novartis Agreement, which we had previously deferred. Although we have recorded net income for the full year ending December 31, 2017 on account of the

deferred revenue recognized in 2017 exceeding our overall expenses, we incurred an operating loss of $14.9 million and a net loss of $9.5 million during the fourth quarter of 2017 and expect to continue to incur significant operating losses for the foreseeable future.

We have devoted substantially all of our financial resources and efforts to the research and development of Fovista and Zimura and preparations for the potential commercial launch of Fovista, including manufacturing scale-up activities. Although we are no longer pursuing the development of Fovista, we expect to continue to incur significant expenses and operating losses over the next few years as we continue the development of Zimura and potentially add to our product portfolio through in-licensing or acquisition of additional product candidates. Our net losses may fluctuate significantly from quarter to quarter and year to year.

Our product candidate Zimura is in clinical development. We expect to continue to incur significant research and development expenses as we pursue the development of Zimura as currently planned. We could also incur additional research and development expenses if we conclude that there is a scientific rationale for potentially developing, or if we undertake the development of Zimura in additional indications, beyond those already in development, and as we evaluate and potentially in-license or acquire, and undertake development of, additional product candidates, including any promising product candidates that emerge from our collaborative gene therapy research programs. Furthermore, if we successfully develop and obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. We are party to an agreement with Archemix that imposes significant milestone payment obligations on us in connection with our achievement of specific clinical, regulatory and commercial milestones with respect to Zimura. It is likely that any future in-licensing or acquisition agreements that we enter into with respect to additional products, product candidates or technologies would include similar obligations.

We expect that we will continue to incur significant expenses as we:

- continue the clinical development of Zimura as currently planned or potentially in other indications if we believe there is a sufficient scientific rationale to pursue such development;
- in-license or acquire the rights to, and pursue the development of, other products, product candidates or technologies;
- pursue our collaborative gene therapy research programs;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing, quality control, quality assurance and scientific personnel, especially if we are successful in acquiring or in-licensing rights to additional products, product candidates or technologies or progressing the clinical development of any of our product candidates or if we decide to establish internal gene therapy capabilities;
- seek marketing approval for any product candidates that successfully complete clinical trials;
- expand our outsourced manufacturing activities or establish commercial operations or sales, marketing and distribution capabilities, if we receive, or expect to receive, marketing approval for any of our product candidates; and
- expand our general and administrative functions to support future growth of the company.

Our ability to become and remain profitable depends on our ability to generate revenue in excess of our expenses. Our ability to generate revenues from product sales is dependent on our obtaining marketing approval for and commercializing our product candidates or any product candidates we may in-license or acquire. We may be unsuccessful in our efforts to develop and commercialize product candidates or in our efforts to in-license or acquire additional product candidates. Even if we succeed in developing and commercializing one or more of our product candidates, we may never achieve sufficient sales revenue to achieve or maintain profitability. See “-Risks Related to Product Development and Commercialization” for a further discussion of the risks we face in successfully developing and commercializing our product candidates and achieving profitability.

We may require substantial, additional funding in order to complete the activities necessary to commercialize one or more of our product candidates. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

As of December 31, 2017, we had cash, cash equivalents and marketable securities of $167.0 million. For 2018, we expect the cash required to fund our operations and capital expenditures, including our Zimura development programs and collaborative gene therapy research programs, as currently planned will range between $50.0 million and $55.0 million. We also had $137.5 million in total liabilities as of December 31, 2017, of which $125.0 million related to the Novo Agreement, which we are required to show as a liability on our balance sheets under generally accepted accounting principles but which does not correspond to any contractual repayment obligation.

We believe that our cash, cash equivalents and marketable securities will be sufficient to fund our operations and capital expenditure requirements as currently planned for at least the next 12 months. This estimate does not reflect any additional expenditures resulting from additional sponsored research or the in-licensing or acquisition of additional product candidates or technologies or associated development that we may pursue following any such transactions. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Our capital requirements will depend on several factors, including the scope of any additional collaborative research programs, the success of our pursuit, by acquisition, in-licensing or otherwise, and subsequent development of additional product candidates or technologies, and the success of our ongoing development programs. We believe that we may need additional funding in the event that we acquire or in-license one or more additional product candidates and undertake development. In addition, our expenses may exceed our expectations if we experience delays in enrollment or with the availability of drug supply for our clinical trials, if we experience any unforeseen issues in our ongoing clinical trials or if we further expand the scope or size of our clinical trials and programs. Our costs may also exceed our expectations for other reasons, for example, if we experience issues with manufacturing or process development, or if we are required by the FDA, the EMA, or regulatory authorities in other jurisdictions to perform clinical or nonclinical trials or other studies in addition to those we currently expect to conduct. As a result, we may need or may seek to obtain additional funding in connection with our continuing operations sooner than expected.

The future development of our product candidates is highly uncertain. We expect the clinical development for Zimura will continue for at least the next several years. At this time, we cannot reasonably estimate the remaining costs necessary to complete clinical development, to complete process development and manufacturing scale-up and validation activities or to potentially seek marketing approval with respect to our product candidates.

Our future capital requirements, therefore, will depend on many factors, including:

- the scope, costs and results of our ongoing Zimura clinical programs, as well as any additional clinical trials we undertake to obtain data sufficient to seek marketing approval for Zimura in any indication;
- the extent to which we in-license or acquire rights to, and undertake research or development of products, product candidates or technologies, including any product candidate or other technologies we may evaluate as part of our collaborative gene therapy research programs;
- the amount of any upfront, milestone payments and other financial obligations associated with the in-license or acquisition of other product candidates;
- the scope, progress, results and costs of preclinical development and/or clinical trials for any other product candidates that we may develop;
- the costs and timing of process development, manufacturing scale-up and validation activities and ongoing stability studies associated with Zimura or any other product candidates that we may develop;
- our ability to establish collaborations on favorable terms, if at all;
- the costs, timing and outcome of regulatory reviews of our product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending intellectual property-related claims;

- the timing, scope and cost of commercialization activities for any of our product candidates if we receive, or expect to receive, marketing approval for a product candidate; and

- subject to receipt of marketing approval, net revenue received from commercial sales of any of our product candidates, after milestone payments and royalty payments that we would be obligated to make.

We do not have any committed external source of funds. Our future commercial revenues, if any, will be derived from sales of any of our product candidates that we are able to successfully develop, which may not be available for at least several years, if at all. In addition, if approved, our product candidates may not achieve commercial success. If that is the case, we will need to obtain substantial additional financing to achieve our business objectives. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Adequate additional financing may not be available to us on acceptable terms, or at all. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we may need or may seek to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our existing stockholders' ownership interests would be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our existing stockholders' rights as holders of our common stock. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, products or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

We and certain of our current and former executive officers have been named as defendants in lawsuits that could result in substantial costs and divert management's attention.

We and certain of our current and former executive officers have been named as defendants in two purported class action lawsuits initiated in 2017 that generally allege that we and certain of our officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the prospects of our Phase 3 trials for Fovista in combination with anti-VEGF agents for the treatment of wet AMD. The members of our Board of Directors have also been named as defendants in a shareholder derivative action initiated on February 7, 2018, which generally alleges that defendants breached their fiduciary duties to our company by adopting a compensation plan that overcompensates the non-employee members of the Board relative to the boards of companies of comparable market capitalization and size. These complaints seek equitable and/or injunctive relief, unspecified damages, attorneys' fees, and other costs. The defendants deny any allegations of wrongdoing and intend to vigorously defend against these lawsuits. We are unable, however, to predict the outcome of these matters at this time. Moreover, any conclusion of these matters in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance would have a material adverse effect on our financial condition and business. In addition, the litigation could adversely impact our reputation and divert management and our Board of Directors' attention and resources from other priorities, including the execution of business plans and strategies that are important to our ability to grow our business, any of which could have a material adverse effect on our business. Additional similar lawsuits might be filed.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revised the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of

21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modification or repeal of many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain how various states will respond to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

Risks Related to Product Development and Commercialization

Companies in our industry face a wide range of challenging activities, each of which entails separate, and in many cases substantial, risk.

The long-term success of our company, and our ability to become profitable as a biopharmaceutical company will require us to be successful in a range of challenging activities, including:

- designing, conducting and successfully completing pre-clinical development activities, including pre-clinical efficacy and IND-enabling studies, for our product candidates or product candidates we are interested in in-licensing or acquiring, including product candidates we may evaluate as part of our collaborative gene therapy research programs;
- designing, conducting and completing clinical trials for our product candidates;
- obtaining favorable results from required clinical trials, including for each ophthalmic product candidate, favorable results from two adequate and well controlled pivotal clinical trials in the relevant indication;
- applying for and receiving marketing approvals from applicable regulatory authorities for the use of our product candidates;
- making arrangements with third-party manufacturers, receiving regulatory approval of our manufacturing processes and our third-party manufacturers' facilities from applicable regulatory authorities and ensuring adequate supply of drug product;
- establishing sales, marketing and distribution capabilities, either internally or through collaborations or other arrangements, to effectively market and sell our product candidates;
- achieving acceptance of the product candidate, if and when approved, by patients, the medical community and third-party payors;
- if our product candidates are approved, obtaining from governmental and third-party payors adequate coverage and reimbursement for our product candidates and, to the extent applicable, associated injection procedures conducted by treating physicians;
- effectively competing with other therapies, including the existing standard of care, and other forms of drug delivery;
- maintaining a continued acceptable safety profile of the product candidate during development and following approval;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity, including under the Orphan Drug Act and the Hatch-Waxman Act, if we choose to seek such protections for any of our product candidates;
- protecting and enforcing our rights in our intellectual property portfolio; and

- complying with all applicable regulatory requirements, including FDA Good Clinical Practices, or GCP, Good Manufacturing Practices, or GMP, and standards, rules and regulations governing promotional and other marketing activities.

Each of these activities has associated risks, many of which are detailed below and throughout this “Risk Factors” section. We may never succeed in these activities and, even if we do, may never generate revenues from product sales that are significant enough to achieve commercial success and profitability. Our failure to be commercially successful and profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or continue our operations. A decrease in the value of our company would also cause our stockholders to lose all or part of their investment.

Drug development is a highly uncertain undertaking. Our development efforts may be delayed for any number of reasons, in which case potential marketing approval or commercialization of our product candidates could be delayed or prevented.

Before obtaining approval from regulatory authorities for the sale of any product candidate, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Prior to initiating clinical trials, a sponsor must complete extensive pre-clinical testing of a product candidate, including, in most cases, pre-clinical efficacy experiments as well IND-enabling toxicology studies. These experiments and studies may be time-consuming and expensive to complete. The necessary pre-clinical testing may not be completed successfully for a pre-clinical product candidate and a potentially promising product candidate may therefore never be tested in humans. Once it commences, clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

We may experience numerous unforeseen events during drug development that could delay or prevent our ability to receive marketing approval or commercialize our product candidates. In particular, clinical trials of our product candidates may produce inconclusive or negative results, such as the results we observed in our pivotal Phase 3 Fovista program for the treatment of wet AMD.

We have limited data regarding the safety, tolerability and efficacy of Zimura administered for the treatment of GA or administered in combination with anti-VEGF drugs for the treatment of wet AMD or IPCV and no data regarding the safety, tolerability and efficacy of Zimura administered for the treatment of STGD1 or non-infectious intermediate and posterior uveitis.

Given that we have limited data regarding the effect of Zimura in GA, we determined the size of the OPH2003 trial in GA based on our best estimates of the size of trial required to demonstrate a potential clinical benefit for Zimura. This estimate incorporates our assumptions regarding the potential performance of Zimura in this indication based in part on available third-party clinical data and our statistical analysis of this data. In addition, we determined the size of the OPH2005 trial in STDG1 based on the number of patients with STGD1 that we believe could potentially be enrolled within a reasonable period of time. This number may be increased or decreased in light of the actual enrollment rate during the trial. As STGD1 is an orphan indication, to our knowledge there is only very limited natural history data currently available regarding the variability for our planned primary efficacy endpoint in the STGD1 patient population we plan to enroll in this trial. Given the information above, these trials could be underpowered to demonstrate a potential clinical benefit for Zimura in these indications.

Furthermore, our current and planned Zimura clinical trials are evaluating or will evaluate Zimura dosing regimens that we have not studied before, which may increase the risk that patients in these trials experience adverse events and/or serious adverse events (either ocular, systemic or both) that we have not observed or at rates that we have not observed in prior trials. For a further discussion of the safety risks in our trials, see the risk factor herein entitled "*If serious adverse or unacceptable side effects are identified during the development of our product candidate, we may need to abandon or limit our development of such product candidate."*

Moreover, the failure of prior clinical trials evaluating complement inhibition in GA, including a competitor's two Phase 3 clinical trials evaluating an investigational anti-complement factor D antibody administered via intravitreal injections, a second competitor's Phase 2 clinical trial evaluating an investigational anti-C5 antibody administered via intravitreal injections and a third competitor's Phase 2 clinical trial evaluating an anti-C5 antibody administered systemically, may call into question the hypothesis underlying the use of a complement inhibitor as a method for treating GA. In addition, the competitor's anti-C5

antibody administered via intravitreal injections that was studied for the treatment of GA did not show any benefit when studied in a cohort of anti-VEGF treatment-experienced wet AMD patients.

Our clinical development programs may fail to produce positive safety or efficacy data that support the use of these product candidates in the indications we are pursuing. Additional development risks include the following:

- we may not be able to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation of clinical studies for any preclinical product candidates that we in-license or acquire;
- regulators or institutional review boards may not agree with our study design, including our selection of endpoints, or may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective clinical research organizations or clinical trial sites, especially in cases where we are working with clinical research organizations or clinical trial sites we have not worked with previously;
- our contract research organizations, clinical trial sites, contract manufacturers and packagers and analytic testing service providers may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we, through our clinical trial sites, may not be able to locate and enroll a sufficient number of eligible patients to participate in our clinical trials as required by the FDA or similar regulatory authorities outside the United States, especially in our clinical trials for orphan or other rare diseases;
- we may decide, or regulators or institutional review boards may require us, to suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements, including GCPs, or a finding that the participants are being exposed to unacceptable health risks;
- as there are no therapies approved for either GA or Stargardt disease in either the United States or the European Union, the regulatory pathway for product candidates in these indications, including the selection of the primary efficacy endpoint for a pivotal clinical trial, is highly uncertain;
- there may be changes in regulatory requirements and guidance or we may have changes in trial design that require amending or submitting new clinical protocols;
- there may be changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- we may decide, or regulators may require us, to conduct additional clinical trials beyond those we currently contemplate or to abandon product development programs;
- the number of patients required for clinical trials of our product candidates to demonstrate statistically significant results may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate. These risks may be heightened for clinical trials in orphan diseases, for which the natural history of the disease is less understood, making it more difficult to predict the drug effect required to adequately demonstrate efficacy, and because there are fewer affected patients available to participate in clinical trials;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or product candidates we are investigating or other materials necessary to conduct clinical trials of our product candidates, such as the anti-VEGF drugs we need to use in combination with Zimura in our wet AMD and IPCV trials, may be insufficient or inadequate or we may face delays in the manufacture and supply of our product candidates as a result of a decision to transfer manufacturing between contract manufacturers or on account of interruptions in our supply chain, including in relation to the packaging and distribution or import / export of clinical materials; and

- we may face delays in the manufacture and supply of any product candidates we are investigating in our collaborative gene therapy research programs as a result of our inability to establish new manufacturing capabilities or processes.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we contemplate, if we are unable to successfully complete clinical trials or of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use limitations, distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Despite our current development plans and ongoing efforts, we may not complete any of our ongoing or planned clinical trials or other clinical trials for our product candidates. Moreover, the timing of the completion of, and the availability of results from, clinical trials is difficult to predict. Furthermore, our development plans may change based on feedback we may receive from regulatory authorities throughout the development process. If we experience delays in testing or marketing approvals, our product development costs would increase. We do not know whether clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

We have no experience in gene therapy clinical development. Our lack of experience may limit our ability to be successful or may delay our development efforts.

Gene therapy is an emerging field of drug development with only one gene replacement therapy having received FDA approval to date. The novel gene therapy delivery technologies and "minigene" therapy approaches we are evaluating in our collaboration with UMMS are particularly early-stage in their development. Even with promising pre-clinical efficacy data for a new gene therapy product candidate, there will remain several areas of drug development risk, including translational science, manufacturing techniques, safety concerns, regulatory pathway, clinical trial design and the approach to ocular gene therapy administration through either sub-retinal surgery or intravitreal delivery, which will likely pose particular uncertainty given the relatively limited development history for gene therapies. Although we believe gene therapy is a promising area for ophthalmic drug development, we do not have any internal gene therapy development experience or specific gene therapy capabilities. In entering this new area, we will need to build significant technical capabilities, including translational, manufacturing, process development, and other capabilities. We will either need to hire internally for these capabilities or establish them through outside service providers. We believe that gene therapy is an area of significant investment by biotechnology and pharmaceutical companies and that there may be a scarcity of talent available to us in these areas. If we are not able to establish our own internal or outsourced gene therapy capabilities, we may not be able to develop promising product candidates that emerge from our collaborative gene therapy research programs, which would limit our prospects for future growth.

If serious adverse or unacceptable side effects are identified during the development of our product candidate, we may need to abandon or limit our development of such product candidate.

If any of our product candidates are associated with serious adverse events or undesirable side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk–benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause side effects that prevented further development of the compound.

We have limited data regarding the safety, tolerability and efficacy of Zimura administered for the treatment of GA or administered in combination with anti–VEGF drugs for the treatment of wet AMD or IPCV and no data regarding the safety, tolerability and efficacy of Zimura administered for the treatment of STGD1 or non-infectious intermediate and posterior uveitis. Our clinical trials for Zimura involve dosing regimens that we have not studied before, which may increase the risk that patients in these trials experience adverse events and/or serious adverse events (either ocular, systemic or both) that we have not observed or at rates that we have not observed in prior trials. In addition, our clinical trials for Zimura will involve multiple intravitreal injections over an extended period of time and, as such, may involve risks regarding multiple and chronic intravitreal injections. For these reasons, there may be, among others, an increase in the rates of intraocular infections, or endophthalmitis, intraocular pressure, glaucoma, retinal tears, cataracts, retinal detachment, intraocular inflammation, retinal and/or choroidal circulation compromise, cardiovascular disease such as myocardial infarctions, stroke, blood clots or emboli, or hospitalizations in patients who receive Zimura monotherapy or Zimura in combination with anti-VEGF therapy. Because we currently have only one product candidate in clinical development, it is possible that a safety issue in any of our ongoing clinical trials for Zimura could impact all of our ongoing clinical trials.

In addition, there are several known safety risks specific to gene therapy, including inflammation resulting from a patient's immune response to the administration of viral vectors and the potential for toxicity as a result of chronic exposure to the expressed protein. In the event that we in-license or acquire a gene therapy product candidate and progress it into clinical development, we may experience delays or other challenges for our development programs as a result of safety issues.

Our experience manufacturing Zimura is limited. We have no experience manufacturing gene therapy product candidates. Manufacturing issues, including technical or quality issues or issues securing capacity, may arise that could cause delays in our development programs or increase costs. In addition, we may experience delays in regulatory approval of our product candidates if we do not satisfy applicable manufacturing regulatory requirements.

We do not have any internal manufacturing facilities, personnel or other capabilities and are dependent on outside contract manufacturers to manufacture Zimura and any other product candidates that we would acquire or in-license as part of pursuing our business plan. Manufacturing for these product candidates could be complicated or present novel technical challenges. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

We currently rely upon a single third-party manufacturer, Agilent Technologies, to supply us with the chemically synthesized API for Zimura and a different, single third-party manufacturer, Ajinomoto Althea, to provide fill/finish services for Zimura. In order to obtain and maintain regulatory approval for Zimura , our third-party manufacturers will be required to consistently produce the API used in Zimura in commercial quantities and of specified quality and to execute fill/finish services on a repeated basis and document their ability to do so. If the third-party manufacturers are unable to satisfy this requirement, our business would be materially and adversely affected. To date, we have not yet scaled up the manufacturing process for Zimura beyond the scale used for developmental clinical batches, nor have we validated the manufacturing process.

These manufacturing processes and the facilities of our third-party manufacturers, including our third-party API manufacturer and our third-party fill/finish service provider, are subject to inspection and approval by the FDA, referred to as a pre-approval inspection, before we can commence the commercial sale of any approved product candidate, and thereafter on an ongoing basis. Our third-party API manufacturer has undergone only one pre-approval inspection by the FDA, and has not yet gone through a pre-approval inspection for Zimura. Our third-party fill/finish service provider is subject to FDA inspection from time to time. Failure by our third-party manufacturers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to our product candidates may result in delays in the approval of our applications for marketing approval in the event a recommendation to withhold is issued, as well as regulatory actions such as the issuance of FDA Form 483 notices of observations, warning letters or injunctions or the loss of operating licenses. Additionally, on October 22, 2014, the FDA issued its final guidance on the circumstances that constitute delaying, denying, limiting or refusing a drug inspection pursuant to Section 707 of the Food and Drug Administration Safety and Innovation Act of 2012. If any of our third-party manufacturers are found to have delayed, denied, limited or refused a drug inspection, our API or drug product could be deemed adulterated. Based on the severity of the regulatory action, our clinical or commercial supply of API or our fill/finish services could be interrupted or limited, which could have a material adverse effect on our business.

Some of the standards of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, which establishes basic guidelines and standards for drug development in the United States, the European Union, Japan and other countries, do not apply to oligonucleotides, including aptamers. As a result, there are no established generally accepted manufacturing or quality standards for the production of Zimura. The lack of uniform

manufacturing and quality standards among regulatory agencies may delay regulatory approval of Zimura or any future product candidate.

In addition, in order to manufacture and supply any of our product candidates on a commercial scale in the future, we will need to bolster our quality control and quality assurance capabilities, including by augmenting our manufacturing processes and adding personnel. We also may encounter problems hiring and retaining the experienced specialist scientific and manufacturing personnel needed to operate our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. As we or any manufacturer we engage scales-up manufacturing of any approved product, we may encounter unexpected issues relating to the manufacturing processes or the quality, purity or stability of the product, and we may be required to refine or alter our manufacturing processes to address these issues. Resolving these issues could result in significant delays and may result in significantly increased costs. If we underestimate the demand for an approved product, given the long lead times required to manufacture or obtain regulatory approvals for our products, we could potentially face commercial drug product supply shortages. If we experience significant delays or other obstacles in producing any approved product at commercial scale, our ability to market and sell any approved products may be adversely affected and our business could suffer.

Gene therapies are complex and difficult to manufacture. A number of factors common to the manufacturing of most biologics and drugs could also cause production interruptions, including raw materials shortages, raw material failures, growth media failures, equipment malfunctions, facility contamination, labor problems, natural disasters, disruption in utility services, terrorist activities, or acts of god beyond our control.

In addition, we believe that because of the high demand for clinical gene therapy material in the industry, and a scarcity of potential contract manufacturers, there may be long lead times for establishing manufacturing capabilities and for manufacturing materials for gene therapy drug development activities, including for GMP material needed for clinical trials. It is often the case that early stage research is conducted with materials that are not manufactured using GMP techniques and are not subject to the same level of analysis that would be required for clinical grade material. Therefore, to the extent that we are in-license or acquire a new gene therapy product candidate, we may need to devote significant time and financial resources to establishing manufacturing processes that are sufficient for clinical supplies. In addition, because early stage, pilot manufacturing is often done on a small scale, we may face challenges scaling up any early stage manufacturing to the scale necessary to support supply for clinical trials. If we are not able to establish gene therapy manufacturing or related processes, our development plans may be delayed or stalled and our business may be materially harmed.

Any problems in our manufacturing process or our third-party contract manufacturers' facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs. Problems in our manufacturing process or facilities also could restrict our ability to meet market demand for our products.

Even if any of our product candidates receives marketing approval, such product candidate may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success and the market opportunity for any of our products and product candidates may be smaller than we estimate.

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current treatments for wet AMD, including Lucentis, Eylea and low cost, off-label use of Avastin, are well established in the medical community, and doctors may continue to rely upon these treatments without Zimura. If any of our product candidates, if approved, do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of Zimura or any other product candidate that we may develop, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments, including the existing standard of care;
- any restrictions in the label on the use of our products in combination with other medications;
- any restrictions in the label on the use of our products by a subgroup of patients;
- restrictions in the label on the use of our combination therapy product candidates, such as Zimura for the treatment of wet AMD or IPCV, limiting their use in combination with particular standard of care drugs, such as a particular anti-VEGF drug;

- restrictions in the label imposing a waiting period in between intravitreal injections;

- our and any commercialization partner's ability to offer our products at competitive prices, particularly in light of the cost of any of our combination therapy product candidates in addition to the cost of the underlying standard of care drug;

- availability of third-party coverage and adequate reimbursement, particularly by Medicare given the target market for AMD indications for persons over age 50;

- increasing reimbursement pressures on treating physicians due to the formation of accountable care organizations and the shift away from traditional fee-for-service reimbursement models to reimbursement based on quality of care and patient outcomes;

- willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, particularly in light of the existing available standard of care or to the extent our product candidates require invasive procedures for administration, such as subretinal surgery;

- prevalence and severity of any side effects or perceived safety concerns, especially for new therapeutic modalities such as gene therapy; and

- whether competing products or other alternatives are more convenient or easier to administer, including whether co-formulated alternatives, alternatives that can be co-administered in a single syringe or alternatives that offer a less invasive method of administration than intravitreal injection come to market.

For each of our Zimura trials where patients will receive multiple intravitreal injections on the same day, either Zimura in combination with an anti-VEGF agent or multiple Zimura injections, we have provided for a delay in the second intravitreal injection to minimize the risk of an unacceptable increase in IOP as a result of the volume of the multiple injections. If Zimura receives marketing approval for a particular indication and the approved label requires a waiting period, the potential market opportunity for Zimura may be limited to the extent that physicians and patients find such a waiting period unacceptable.

In addition, the potential market opportunity for any product candidate is difficult to estimate precisely. Our estimates of the potential market opportunity for our product candidates include several key assumptions based on our expectations of the safety and effectiveness of the relevant product candidate, our industry knowledge, industry publications, market response to marketed AMD drugs, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions and any of these assumptions could prove to be inaccurate, and the actual market for such product candidates could be smaller than our estimates of our potential market opportunity.

With respect to our programs for orphan diseases, our understanding of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of these diseases. The number of patients in the United States, the European Union and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our products or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects.

We face substantial competition, which may result in others developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our product candidates from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies, as well as generic and biosimilar companies, worldwide. There are a number of pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of GA, wet AMD, Stargardt disease, non-infectious intermediate and posterior uveitis or other disease indications for which we may develop Zimura. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. We also will face similar competition with respect to any other products or product candidates that we may seek to develop or

commercialize in the future. In particular, many companies are pursuing gene therapy approaches for age-related and orphan retinal diseases.

Our commercial opportunity could be reduced or eliminated if one or more of our competitors develop and commercialize products that are more effective, safer, have fewer or less severe side effects, are more convenient to use or are less expensive than our product candidates. The method of administration of Zimura, intravitreal injection, is commonly used to administer ophthalmic drugs for the treatment of severe disease and is generally accepted by patients facing the prospect of sever visual loss or blindness. A therapy that offers a less invasive method of administration, however, might have a competitive advantage over one administered by intravitreal injection, depending on the relative safety of the other method of administration.

Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the relevant market. Furthermore, our ability to compete may be affected in many cases by insurers or other third-party payors, particularly Medicare, seeking to encourage the use of less expensive or more convenient products.

Competitive considerations for Dry AMD and GA:

- There are a number of products in preclinical research and clinical development by third parties to treat dry AMD, including several that are in development for GA secondary to dry AMD. In general, these product candidates can be categorized based on their proposed mechanisms of action. The mechanisms of action for these product candidates include inflammation suppression, such as complement system inhibitors and corticosteroids, visual cycle modulators, antioxidants and neuroprotectants, cell and gene therapies and vascular perfusion enhancers. Based on publicly available information, we are aware that Novartis AG and MorphoSys AG, Apellis Pharmaceuticals, Inc., Hemera Biosciences, Inc., Achillion Pharmaceuticals, Inc. and Catalyst Biosciences, Inc. each have complement inhibitors in development, the most advanced of which we believe is Apellis's pegylated, synthetic peptide targeting complement factor C3. Apellis announced positive Phase 2 results for its product candidate and has announced plans to initiate a Phase 3 program during 2018. If Apellis's Phase 3 program for its complement factor C3 product candidate is successful, it is likely that Apellis may obtain marketing approval for its product candidate in advance of when we could reasonably expect marketing approval for Zimura in GA, if at all. Moreover, based on publicly available information, we are aware that several other companies have announced development programs for the treatment of dry AMD targeting different mechanisms of action outside of the complement system.

Competitive considerations for wet AMD:

- There are a number of products in preclinical research and clinical development by third parties to treat wet AMD. Based on publicly available information, we are aware that multiple mechanisms of action are in clinical or pre-clinical development for wet AMD, including Angiopoietin-2 inhibitors, tyrosine kinase inhibitors, integrin inhibitors, novel VEGF inhibitors and complement inhibitors, as well as a few remaining PDGF inhibitors. Within the complement system, we are aware that Apellis is planning a Phase 2 clinical trial with their C3 inhibitor in combination with anti-VEGF therapy. Moreover, based on publicly available information, we are aware that several companies and research organizations are pursuing treatments targeting other molecular targets, potential gene therapy treatments and stem cell transplant treatments for the treatment of wet AMD. In addition, other companies are undertaking efforts to develop technologies to allow for topical dosing of therapeutic agents such as anti-VEGF agents or integrin inhibitors through eye-drops or to allow for a less frequent intravitreal dosing schedule than currently used for standard of care anti-VEGF agents.

- The commercial opportunity for Zimura in wet AMD in particular also could be reduced or eliminated if our competitors develop and commercialize products that reduce or eliminate the use of anti-VEGF drugs for the treatment of patients with wet AMD, since we are only developing Zimura for wet AMD as a combination therapy with anti-VEGF agents. Moreover, we expect that if Zimura is approved for combination therapy for the treatment of wet AMD, the cost of combination treatment would be higher than the cost of treatment of wet AMD with Lucentis, Eylea or particularly Avastin monotherapy. Insurers and other third-party payors may encourage the use of anti-VEGF drugs as monotherapy and discourage the use of Zimura in combination with these drugs. This could limit sales of Zimura for this indication.

Competitive considerations for Stargardt disease:

- There are a number of products in preclinical research and clinical development by third parties to treat Stargardt disease. Based on publicly available information, we are aware that Sanofi, Acucela Inc., Alkeus Pharmaceuticals, Inc., Vision Medicines, Inc., Lin BioScience, Inc., Nightstar Therapeutics plc and ProQR Therapeutics N.V. each have development programs in Stargardt disease. Four of these programs, Acucela, Alkeus, Vision Medicines and Lin BioScience, are exploring the use of oral therapeutics, while Sanofi, with technology provided by Oxford BioMedica plc, and Nightstar are each using a gene therapy approach and ProQR is using an RNA interference approach. Acucela's, Alkeus's and Sanofi's product candidates are each in Phase 2 development.

- In the case of orphan diseases such as Stargardt disease, should we be successful in development, our commercialization efforts may rely on non-patent market exclusivity periods under the Orphan Drug Act and the Hatch-Waxman Act. The Orphan Drug Act only provides exclusivity periods for the specific drug granted orphan designation for a specific indication. In addition, there are limited circumstances under each of the Orphan Drug Act and the Hatch-Waxman Act that could result in our loss of data and marketing exclusivity, which could allow a competitor to enter the market. Failure to maintain either data or market exclusivity period would have a material adverse effect on our ability to commercialize our product candidates.

Many of our competitors have significantly greater financial and human resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient enrollment for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our clinical development programs.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing any of our product candidates that we develop if and when any such product candidate is approved.

As a company, we have no experience in the sale, marketing or distribution of pharmaceutical products. We currently do not have any sales, marketing or distribution infrastructure. To achieve commercial success for any approved product, we must either develop a sales, marketing and distribution organization or outsource those functions to third parties. We expect that our commercial strategy for any of our product candidates, including whether to retain commercial rights and market and sell the product candidate ourselves or to utilize collaboration, distribution or other marketing arrangements with third parties, would be determined based on a variety of factors, including the size and nature of the patient population, the disease area, the particular indication, the territory in which the product candidate may be marketed and the commercial potential for such product candidate. In addition, our commercial strategy would vary depending on whether the disease is typically treated by general ophthalmology practitioners, specialists, such as retinal specialists, or sub-specialists.

There are risks involved with establishing our own sales, marketing and distribution capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;

- the inability of sales personnel to obtain access to adequate numbers of physicians who may prescribe our products;

- the lack of complementary products to be offered by our sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and

- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues and our profitability, if any, are likely to be lower than if we were to market, sell and distribute ourselves any products that we develop. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we would not be successful in commercializing our product candidates.

Even if we are able to commercialize any of the product candidates that we may develop, the product may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Health care reform is an issue of intense political focus, particularly in the United States. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals or in ways that could alter the mechanism by which pharmaceutical prices are negotiated or otherwise determined. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control or negotiation even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our or any commercialization partner's commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval and are widely accepted and prescribed or used by physicians.

Our ability and the ability of any commercialization partner to commercialize a product candidate successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A major trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors, particularly Medicare, have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications and encouraging the substitution of lower cost or generic products. Pricing pressures recently experienced by the pharmaceutical industry may be further exacerbated by legislative and policy changes under consideration by the Trump Administration. For example, the new Administration has expressed an interest in authorizing and/or directing the Center for Medicare & Medicaid Service or other agencies of the U.S. government to negotiate prices for drugs covered by Medicare directly with pharmaceutical companies. If this were to occur, especially for wet AMD drugs where a large portion of the patient population is over the age of 65 and is therefore covered by Medicare, there could be significant downward pressure on prices charged, not only for patients covered by Medicare, but also for patients covered by private insurers who may follow the government's lead on price. Moreover, increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize or any commercialization partner commercializes on our behalf, and, even if these are available, the level of reimbursement may not be satisfactory.

Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician and because, in the case of Zimura for the treatment of wet AMD or IPCV, our drug would be administered in combination with other drugs that may carry high prices. In addition, physicians, patients and third-party payors may be sensitive to the addition of the cost of Zimura to the cost of treatment with anti-VEGF drugs for the treatment of wet AMD or IPCV. We or any commercialization partner may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies, including in the case of Zimura for the treatment of wet AMD or IPCV, relative to monotherapy with anti-VEGF drugs. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if

applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States, a policy that President Trump has expressed interest in pursuing. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our and any commercialization partner's inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

The pricing of prescription pharmaceuticals is subject to governmental control outside of the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or a commercialization partner may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Product liability lawsuits against us or any future commercialization partner could divert resources, cause us to incur substantial liabilities and limit commercialization of any products that we may develop or in-license.

We face an inherent risk of product liability exposure related to the testing of any product candidate that we develop in human clinical trials, and we and any future commercialization partner will face an even greater risk if we commercially sell any products that we develop or in-license. Because our Zimura wet AMD and IPCV trials involve or will involve the administration of Zimura in combination with an anti-VEGF drug, we also face an inherent risk of product liability exposure related to the testing of such anti-VEGF drug. If we become subject to or otherwise cannot successfully defend ourselves against claims that our product candidates, anti-VEGF drugs administered in combination with our product candidates or our products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop or in-license;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced time and attention of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop or in-license.

We currently hold $10.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $10.0 million, which may not be adequate to cover all liabilities that we may incur. We will need to increase our insurance coverage when and if we begin commercializing an approved product. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. In addition, if a commercialization or collaboration partner were to become subject to product liability claims or were unable to successfully defend themselves against such claims, any such commercialization or collaboration partners could be more likely to terminate such relationship with us and therefore substantially limit the commercial potential of our products.

Risks Related to Our Dependence on Third Parties

If we are not able to establish collaborations to advance our development programs, we may have to alter our development and commercialization plans.

The development and potential commercialization of our product candidates is likely to require substantial additional cash to fund expenses. In addition, the commercialization of a product candidate in markets outside of the United States requires regulatory expertise and commercial capabilities that are specific to the local market. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

We may enter into collaborations with third parties for the development or commercialization of our product candidates. These collaborations carry numerous risks. If any of our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We may utilize a variety of types of collaboration, distribution and other marketing arrangements with third parties to commercialize our product candidates, either in the United States, or in markets outside the United States. We also may seek third-party collaborators for development and commercialization of other product candidates we may develop. Our likely collaborators for any sales, marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we do enter into any additional arrangements with third parties in the future, we would likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates could pose numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;

- collaborators may deemphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus, changes in product candidate priorities or available funding or changes in priorities as a result of a merger, acquisition or other corporate restructuring or transaction;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;

- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;

- we could grant exclusive rights to our collaborators, which would prevent us from collaborating with others;

- disagreements or disputes with collaborators, including disagreements or disputes over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of products or product candidates, might lead to additional responsibilities for us with respect to product candidates or might result in litigation or arbitration, any of which would divert management attention and resources, be time-consuming and be expensive;

- collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;

- collaborators may not properly maintain or defend our intellectual property rights, may infringe the intellectual property rights of third parties, may misappropriate our trade secrets or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation and potential liability; and

- collaborations may be terminated for the convenience of the collaborator, our breach of the terms of the collaboration or other reasons and, if terminated, we may need to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If a collaborator of ours were to be involved in a business combination or other transaction, the foregoing risks would be heightened, and the business combination or transaction may divert attention or resources or create competing priorities. The collaborator may delay or terminate our product development or commercialization program. If one of our collaborators terminates its agreement with us, we could find it more difficult to attract new collaborators and the perception of our company in the business and financial communities could be adversely affected.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

We rely, in part, on third-party researchers to advance our pipeline expansion efforts. These arrangements may not ultimately yield any promising product candidates for clinical development.

Part of our pipeline expansion strategy involves collaborative sponsored research to be performed by third-party research institutions. Although we seek to direct this research and advise on the design of these projects as well as critical development decisions, this research is being performed by individuals that are not our employees and the timeline and quality of the research efforts are outside of our direct control. Academic investigators and other researchers may have different priorities than we do as a biopharmaceutical drug development company. Confidential information and new inventions derived from these research efforts may be disclosed through publications or other means prior to our being able to protect such intellectual property through the filing of patent applications. Our third-party research partners may not be able to obtain or maintain full ownership of inventions that are derived from the research or associated rights, which may limit their ability to provide us with a license to all relevant intellectual property on terms and conditions that are acceptable to us. Even if our collaborative research efforts yield promising results or new technological advances, they may not ultimately result in our being able to develop or exploit the resulting intellectual property.

We rely upon third parties in conducting our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We have in the past and expect in the future to rely upon third parties, such as CROs, clinical data management organizations, biostatisticians, medical institutions (including reading centers) and clinical investigators, in conducting our pre-clinical testing and clinical trials for our product candidates. We or these third parties may terminate their engagements with us

at any time for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our product development activities could potentially be delayed and could potentially be very costly.

Our reliance on these third parties for pre-clinical testing and clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with GCPs for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we would not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and would not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors.

We also rely upon other third parties to store, package, label and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of our Zimura for clinical trials and expect to continue to do so in connection with its potential commercialization and for clinical trials and commercialization of any other product candidates that we may develop. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of Zimura and have limited personnel with manufacturing experience. We currently rely upon and expect to continue to rely upon third-party contract manufacturers to manufacture preclinical and clinical supplies of product candidates we are developing or may develop and commercial supplies of products if and when approved for marketing by applicable regulatory authorities. Our current and anticipated future dependence upon others for the manufacture of the product candidates that we are developing or may develop may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis. In addition, any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval.

We currently rely exclusively upon a single third-party manufacturer to provide supplies of Zimura API and a different single third-party manufacturer to provide fill/finish services for Zimura. Although we have agreements in place with Agilent for the supply of Fovista API and with Althea for clinical and commercial fill/finish services, we do not currently have any contractual commitments for the supply of Zimura API. We also do not currently have arrangements in place for redundant supply or a second source for API for Zimura or for a redundant supply or a second source for fill/finish services. We purchase the proprietary polyethylene glycol, or PEG, reagent used to modify the chemically synthesized aptamer in Zimura on a purchase order basis from a single third-party supplier. We do not currently have any contractual commitments for supply of the PEG reagent we use for Zimura. The prices for manufacturing activities that are not yet contractually committed may vary substantially over time and adversely affect our financial results. Furthermore, we and our contract manufacturers currently rely upon sole-source suppliers of certain raw materials and other specialized components of production used in the manufacture and fill/finish of each of Zimura. We currently expect to rely on third-party manufacturers for any manufacturing needs for our collaborative gene therapy research programs or future gene therapy clinical trials.

If any of our third-party manufacturers fail to fulfill our purchase orders, or if any of these manufacturers should become unavailable to us for any reason, including as a result of capacity constraints, financial difficulties or insolvency, we believe that there are a limited number of potential replacement manufacturers, and we likely would incur added costs and delays in identifying or qualifying such replacements. We could also incur additional costs and delays in identifying or qualifying a replacement manufacturer for fill/finish services if our existing third-party fill/finish provider should become unavailable for any reason. We may be unable to establish agreements with such replacement manufacturers or fill/finish providers or to do so on acceptable terms.

Reliance on third-party manufacturers entails additional risks, including:

- our product candidates may compete with other product candidates and products for access to a limited number of suitable manufacturing facilities that operate under current good manufacturing practices, or cGMP, regulations;
- reliance on the third party for regulatory compliance, quality assurance and quality control;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products and harm our business and results of operations.

We depend on licenses and sublicenses for development and commercialization rights to Zimura. We may enter into similar arrangements with respect to future product candidates. Termination of these rights or the failure by us or our licensees, including our commercialization or collaboration partners to comply with obligations under these or other agreements could materially harm our business and prevent us from developing or commercializing our products and product candidates.

We are party to a license agreement with Archemix on which we depend for rights to Zimura. This agreement imposes diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. Generally, the diligence obligations contained in the agreement require us to use commercially reasonable efforts to develop, seek regulatory approval for and commercialize Zimura in the United States, the European Union, Japan and such other markets where it would be commercially reasonable to do so. Under our license agreement with Archemix we would not be able to avoid our payment obligations even if we believed a licensed patent right was invalid or unenforceable because the license agreements provide that our licenses to all licensed patent rights would terminate if we challenge the validity or enforceability of any licensed patent right. We expect to enter into acquisition or licensing agreements in the future that would impose similar obligations on us, particularly as we pursue our business plan to acquire or in-license additional products, product candidates or other technologies and expand our product pipeline.

If we fail to comply with our obligations under current or future acquisition and licensing agreements, or otherwise breach an acquisition or licensing agreement as a result of our own actions or inaction or the actions or inactions of our commercialization or collaboration partners, our counterparties may have the right to terminate these agreements, in which event we might not have the rights or the financial resources to develop, manufacture or market any product that is covered by these agreements. Our counterparties also may have the right to convert an exclusive license to non-exclusive in the territory in which we fail to satisfy our diligence obligations, which could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or restated agreements with less favorable terms, seek alternative sources of financing or cause us to lose our rights under these agreements, including our rights to Zimura and other important intellectual property or technology. Any of the foregoing could prevent us from commercializing Zimura or other product candidates we may develop, which could have a material adverse effect on our operating results and overall financial condition.

In addition to the above risks, certain of our intellectual property rights are sublicenses under intellectual property owned by third parties, in some cases through multiple tiers. The actions of our licensors may therefore affect our rights to use our sublicensed intellectual property, even if we are in compliance with all of the obligations under our license agreements. For example, the licenses from Archemix include sublicenses to us of rights to specified technology, which we refer to as the SELEX technology, licensed by University License Equity Holdings, Inc. to Gilead Sciences, Inc., or Gilead, and sublicensed by Gilead to Archemix, as well as other technology owned by Gilead and licensed to Archemix. Should our licensors or any of their upstream licensors fail to comply with their obligations under the agreements pursuant to which they obtain the rights that are sublicensed to us, or should such agreements be terminated or amended, our ability to develop and commercialize Zimura and other product candidates may be materially harmed. While the applicable agreements may contain contractual provisions

that would in many instances protect our rights as a sublicensee in these circumstances, these provisions may not be enforceable and may not protect our rights in all instances. Further, we do not have the right to control the prosecution, maintenance and enforcement of all of our licensed and sublicensed intellectual property, and even when we do have such rights, we may require the cooperation of our licensors and their upstream licensors, which may not be forthcoming. Our business could be materially adversely affected if we are unable to prosecute, maintain and enforce our licensed and sublicensed intellectual property effectively.

Risks Related to Our Intellectual Property

The patent prosecution process is expensive and time-consuming, is highly uncertain and involves complex legal and factual questions. Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing in the United States and in certain foreign jurisdictions patent applications related to our novel technologies and product candidates that are important to our business.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. In addition, we may not pursue or obtain patent protection in all major markets. Moreover, in some circumstances, we do not have the right to control the preparation, filing or prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties or covering technology that a collaboration or commercialization partner may develop, the eventual commercialization of which could potentially entitle us to royalty payments. In some circumstances, our licensors have the right to enforce the licensed patents without our involvement or consent, or to decide not to enforce or to allow us to enforce the licensed patents. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If any such licensors fail to maintain such patents, or lose rights to those patents, the rights that we have licensed may be reduced or eliminated and our ability to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign jurisdictions may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. Moreover, the U.S. Patent and Trademark Office, or USPTO, might require that the term of a patent issuing from a pending patent application be disclaimed and limited to the term of another patent that is commonly owned or names a common inventor. As a result, the issuance, scope, validity, term, enforceability and commercial value of our patent rights are highly uncertain.

Our pending and future patent applications, and any collaboration or commercialization partner’s pending and future patent applications, may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. In particular, during prosecution of any patent application, the issuance of any patents based on the application may depend upon our or their ability to generate additional preclinical or clinical data that support the patentability of our proposed claims. We or any collaboration or commercialization partner may not be able to generate sufficient additional data on a timely basis, or at all. Moreover, changes in either the patent laws or interpretation of the patent laws in the United States or other countries may diminish the value of our or a collaboration or commercialization partner’s patents or narrow the scope of our or their patent protection.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art, may affect patent litigation and switch the U.S. patent system from a “first-to-invent” system to a “first-to-file” system. Under a first-to-file system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The USPTO

recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first-to-file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Moreover, we may be subject to a third-party preissuance submission of prior art to the USPTO, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review, interference proceedings or other patent office proceedings or litigation, in the United States or elsewhere, challenging our patent rights or the patent rights of others. Based on available information, we believe that *inter partes* review proceedings, brought by financial investors who may be selling short the stock of the patent holder, are becoming more prevalent. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights; allow third parties to commercialize our technology or products and compete directly with us, without payment to us; or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

If we are unable to obtain and maintain or do not maintain patent protection for our technology and products during the period of their commercialization, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be adversely affected.

The U.S. patent rights covering Zimura as a composition of matter are expected to expire in 2025. The U.S. patent rights covering methods of treating certain complement protein mediated disorders with Zimura are expected to expire in 2026. The European patent rights covering the composition of matter of Zimura and methods of treating certain complement protein mediated disorders with Zimura are expected to expire in 2025. As we expect the clinical development of Zimura to continue for at least the next several years, these expiration dates may be prior to the date by which we would be able to commercialize Zimura in the United States or Europe if we seek and obtain marketing approval. Once our patents expire, we may not be able to exclude competitors from commercializing products similar or identical to ours if such competitors do not use or promote our claimed methods of treatment or do use or promote our methods of treatment after our patents expire.

Depending on potential delays in the regulatory review process for Zimura, we may be able to obtain patent term restoration for one of our patents in the United States under the Hatch-Waxman Act, which permits a patent restoration term of up to five years as partial compensation for patent term effectively lost during product development and the FDA regulatory review process occurring after the issuance of a patent, but we can provide no assurances that such a restoration term will be obtained. Similar to the patent term restoration available in the United States, the regulatory framework in the European Union and certain other foreign jurisdictions provides the opportunity to extend the term of a patent that covers an approved drug in certain circumstances. Notwithstanding the availability of patent term extension or restoration provisions, we may not be granted patent term extensions because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term or scope of any such extension is less than we request, any period during which we have the right to exclusively market our product would be shorter than we would otherwise expect, and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

Certain of our licensed patent rights for Zimura are method-of-treatment patents. Method-of-treatment patents are more difficult to enforce than composition-of-matter patents because of the risk of off-label sale or use of a drug for the patented method. The FDA does not prohibit physicians from prescribing an approved product for uses that are not described in the product’s labeling. Although use of a product directed by off-label prescriptions may infringe our method-of-treatment patents, the practice is common across medical specialties, particularly in the United States, and such infringement is difficult to detect, prevent or prosecute. Off-label sales of other products having the same API as Zimura or any other product candidates we may develop would limit our ability to generate revenue from the sale of Zimura or such other product candidates, if approved for commercial sale. In addition, European patent law generally makes the issuance and enforcement of patents that cover methods of treatment of the human body difficult. Further, once the composition-of-matter patents relating to Zimura or any other product candidate in a particular jurisdiction, if any, expire, competitors will be able to make, offer and sell products containing the same API as Zimura or such other product candidate in that jurisdiction so long as these competitors do not infringe any other of our patents covering Zimura’s composition of matter or method of use or manufacture, do not violate the terms of any marketing or data exclusivity that may be granted to us by regulatory authorities and obtain any necessary

marketing approvals from applicable regulatory authorities. In such circumstances, we also may not be able to detect, prevent or prosecute off-label use of such competitors' products containing the same API as Zimura, even if such use infringes any of our method-of-treatment patents.

The Hatch-Waxman Act also permits the manufacture, use, offer for sale, sale or importation of a patented invention other than a new animal drug or veterinary biological product, if the manufacture, use, offer for sale, sale or importation is solely for uses that are reasonably related to development of information that could be submitted to the FDA. For this reason, our competitors might be able under certain circumstances to perform activities within the scope of the U.S. patents that we own or under which we are licensed without infringing such patents. This might enable our competitors to develop during the lifetime of these patents drugs that compete with our product candidates, if they are ultimately approved.

Our issued patents may not be sufficient to provide us with a competitive advantage. For example, competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. Even if our owned or licensed patent applications issue as patents, they may not issue with a scope broad enough to provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. We could also fail to take the required actions and pay the necessary governmental fees to maintain our patents.

The issuance of a patent is not conclusive as to its inventorship, ownership, scope, term, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. For example, if we receive marketing approval for our product candidates, other pharmaceutical companies may seek approval of generic versions of our products with the FDA or regulatory authorities in other jurisdictions. We may then be required to initiate proceedings against such companies in order to enforce our intellectual property rights. The risk of being involved in such proceedings is likely to increase if our products are commercially successful. In any such proceedings, the inventorship, ownership, scope, term, validity and enforceability of our patents may be challenged. These and other challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to prevent others from using or commercializing similar or identical technology and products or from launching generic versions of our products, or could limit the duration of the patent protection of our technology and products. The launch of a generic version of one of our products in particular would be likely to result in an immediate and substantial reduction in the demand for our product, which could have a material adverse effect on our business. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe or otherwise violate our patents, trademarks, copyrights or other intellectual property. To counter infringement or other violations, we may be required to file claims, which can be expensive and time consuming. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights. In addition, in a patent infringement proceeding, a court may decide that one or more of the patents we assert is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to prevent the other party from using the technology at issue on the grounds that our patents do not cover the technology. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In such a case, we could ultimately be forced to cease use of such marks. In any intellectual property litigation, even if we are successful, any award of monetary damages or other remedy we receive may not be commercially valuable. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Third parties may initiate legal proceedings or take other actions alleging that we are infringing or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of any future collaboration and commercialization partners to develop, manufacture, market and sell our product candidates and products and use our proprietary technologies without infringing or otherwise violating the intellectual property and other proprietary rights of third parties. New patent applications in the filed of biotechnology and pharmaceuticals, and gene therapies in particular, are being filed at a rapid pace.

There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We or any future collaboration and commercialization partners may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference, derivation, re-examination, post-grant review, *inter partes* review, opposition, cancellation or similar proceedings before the USPTO or its foreign counterparts. The risks of being involved in such litigation and proceedings may also increase as our or their product candidates near commercialization.

Third parties may assert infringement claims against us or our collaboration or commercialization partners based on existing or future intellectual property rights. We or they may not be aware of all such intellectual property rights potentially relating to our product candidates and their manufacture and uses. There is a lag between the filing of a patent application, which generally establishes the priority date of a patent claim, and the publication of such patent application. During the period between filing of a patent application and publication of the application, we would not otherwise have a means of discovering the existence or extent of the claimed inventions contained in a filed but unpublished patent application. Patent applications are often drafted broadly, and the scope of patent claims that may ultimately issue may not be known until several years after a patent application is filed and published. We may make development or pipeline decisions based on our belief that our product candidates can be distinguished from patent claims contained in published patent applications or issued patents, that patent claims contained in published patent applications are unlikely to issue as drafted, or that claims contained in issued patents are invalid. These positions regarding third-party intellectual property may not ultimately be successful in litigation. Thus, we do not know with certainty that our product candidates, or our intended commercialization thereof, does not and will not infringe or otherwise violate any third party's intellectual property.

If we are or any of our future collaboration or commercialization partners is found to infringe or otherwise violate a third party's intellectual property rights, we or they could be required to obtain a license from such third party to continue developing and marketing our or their products and technology or to continue using a trademark. However, we or our future collaboration and commercialization partners may not be able to obtain any required license on commercially reasonable terms or at all. Even if we or they were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our collaboration and commercialization partners and could require us or them to make substantial licensing and royalty payments. We or our future collaboration and commercialization partners could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us or our future collaboration and commercialization partners from commercializing our or their product candidates or force us or them to cease some of our business operations, which could materially harm our business. Claims that we or our future collaboration and commercialization partners have misappropriated the confidential information or trade secrets of third parties could expose us or them to similar liabilities and have a similar negative impact on our business.

We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees and contractors were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees and contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees or contractors have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's or contractor's former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact conceives or develops intellectual property that we regard as our own. Moreover, because we acquired rights to Zimura from Archemix, we must rely upon Archemix's and its successors' practices, and those of its predecessors, with regard to the assignment of intellectual property therein. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel.

Intellectual property litigation could cause us to spend substantial resources and could distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by governmental patent offices, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and patent offices in foreign countries in several stages over the lifetime of the patent. The USPTO and patent offices in foreign countries require compliance with a number of procedural, documentary, fee payment and other requirements during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of a patent or patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and products, we also rely upon trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. We cannot guarantee that we have executed such agreements with each party that may have or have had access to our trade secrets. Moreover, because we acquired certain rights to Zimura from Archemix, we must rely upon Archemix's and its successors' practices, and those of its predecessors, with regard to the protection of Zimura-related trade secrets before we acquired it. Any party with whom we or they have executed a non-disclosure and confidentiality agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Our proprietary information may also be obtained by third parties by other means, such as breaches of our physical or computer security systems.

Detecting the disclosure or misappropriation of a trade secret and enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Regulatory Approval and Marketing of our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue would be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and

distribution, export and import, are subject to comprehensive regulation by the FDA and by the EMA and comparable regulatory agencies in other countries.

In general, the FDA and similar regulatory authorities outside the United States require two adequate and well controlled clinical trials demonstrating safety and effectiveness for marketing approval for an ophthalmic pharmaceutical product. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely upon third-party CROs to assist us in this process. Securing marketing approval requires obtaining positive safety and efficacy data from required clinical trials, as well as the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authorities. The FDA or other regulatory authorities may determine that a product candidate that we may develop is not effective, is only moderately effective or has undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use. In the case of Zimura for the treatment of wet AMD or IPCV, the FDA or other regulatory authority may limit the approval of Zimura to use with only specified anti-VEGF drugs that are approved for the treatment of wet AMD or IPCV rather than with all anti-VEGF drugs. Such limitation could limit sales of Zimura for the treatment of wet AMD or IPCV.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Marketing approval of novel product candidates such as Zimura manufactured using novel manufacturing processes can be more expensive and take longer than for other, more well-known or extensively studied pharmaceutical or biopharmaceutical products, due to regulatory agencies' lack of experience with them. We believe that the FDA has only granted marketing approval for one aptamer product to date. This lack of experience may lengthen the regulatory review process, require us to conduct additional studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these product candidates or lead to significant post-approval limitations or restrictions.

Accordingly, if we or our collaborators experience delays in obtaining approval or if we fail to obtain approval of Zimura or any other product candidate that we develop, the commercial prospects for such product candidate may be harmed and our ability to generate revenues would be materially impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in such jurisdictions.

In order to market and sell our product candidates in the European Union and many other jurisdictions, we or our third-party commercialization partners must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional preclinical or clinical testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or our third-party commercialization partners may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We and our third-party commercialization partners may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

We currently do not have orphan drug designations or orphan drug exclusivity for any product. If our competitors are able to obtain orphan drug exclusivity for products that constitute the same drug and treat the same indications as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than 5 in 10,000 persons in the European Union. Additionally, orphan designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biologic product.

If we request orphan drug designation for any of our product candidates in one or more indications, there can be no assurances that the FDA or the European Commission will grant any of our product candidates such designation. Additionally, the designation of any of our product candidates as an orphan product does not guarantee that any regulatory agency will accelerate regulatory review of, or ultimately approve, that product candidate, nor does it limit the ability of any regulatory agency to grant orphan drug designation to product candidates of other companies that treat the same indications as our product candidates prior to our product candidates receiving exclusive marketing approval.

Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the European Commission from approving another marketing application for a product that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances. If another sponsor receives such approval before we do (regardless of our orphan drug designation), we will be precluded from receiving marketing approval for our product for the applicable exclusivity period. The applicable period is seven years in the United States and 10 years in the European Union. The exclusivity period in the United States can be extended by six months if the sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be revoked if any regulatory agency determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same condition. In the United States, even after an orphan drug is approved, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is not the same drug or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In the European Union, marketing authorization may be granted to a similar medicinal product for the same orphan indication if:

- the second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;

- the holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or

- the holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

A fast track designation or grant of priority review status by the FDA may not actually lead to a faster development or regulatory review or approval process. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

If a drug is intended for the treatment of a serious or life-threatening disease or condition and the drug demonstrates the potential to address unmet medical needs for this disease or condition, the drug sponsor may apply for FDA fast track designation. If a drug offers major advances in treatment, the drug sponsor may apply for FDA priority review status. The FDA has broad discretion whether or not to grant fast track designation or priority review status, so even if we believe a particular product candidate is eligible for such designation or status the FDA could decide not to grant it. Even though a product has received fast track designation and may be eligible for priority review status, a sponsor may not ultimately experience a faster development process, review or approval compared to conventional FDA procedures.

A breakthrough therapy designation by the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates would receive marketing approval.

We may seek a breakthrough therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interactions and communications between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Any product candidate for which we obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market and we or our third-party commercialization partners may be subject to penalties if we or our third-party commercialization partners fail to comply with regulatory requirements or if we or our third-party commercialization partners experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we or our commercialization partners obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control and quality assurance, complaints and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or may be subject to significant conditions of approval or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy.

The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we

may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on distribution or use of a product;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; and
- litigation involving patients using our products.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Our and our potential commercialization partners' relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us and our commercialization partners to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third-party payors may expose us and our commercialization partners to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we and our commercialization partners market, sell and distribute any products for which we or they obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in

return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $5,500 to $11,000 per false claim;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals, with data collection beginning in August 2013; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our financial results. We are developing and implementing a corporate compliance program designed to ensure that we will market and sell any future products that we successfully develop from our product candidates in compliance with all applicable laws and regulations, but we cannot guarantee that this program will protect us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our or our commercialization partners' operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us or them, we or they may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our or their operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The efforts of the Trump Administration to pursue regulatory reform may limit the FDA's ability to engage in oversight and implementation activities in the normal course, and that could negatively impact our business.

The Trump Administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. On January 30, 2017, President Trump issued an executive order, applicable to all executive agencies, including the FDA, which requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management and Budget on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

In March 2010, President Barack H. Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA. Among the provisions of the ACA of potential importance to our business and our product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription products and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report product samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2025 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional

reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Since enactment of the ACA, there have been numerous legal challenges and congressional actions to repeal and replace provisions of the law. In May 2017, the U.S. House of Representatives passed legislation known as the American Health Care Act of 2017. Thereafter, the Senate Republicans introduced and then updated a bill to replace the ACA known as the Better Care Reconciliation Act of 2017. The Senate Republicans also introduced legislation to repeal the ACA without companion legislation to replace it, and a "skinny" version of the Better Care Reconciliation Act of 2017. In addition, the Senate considered proposed healthcare reform legislation known as the Graham-Cassidy bill. None of these measures was passed by the U.S. Senate.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Administration announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

More recently, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. The Congress will likely consider other legislation to replace elements of the ACA during the next congressional session.

We will continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business. It is possible that repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates. While the timing and scope of any potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provisions.

The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired. In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs.

Finally, legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any future collaborators to more stringent product labeling and post-marketing testing and other requirements.

We are subject to U.S. and foreign anti-corruption and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We are subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and possibly other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. In addition, we may engage third party intermediaries to promote our clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

Noncompliance with anti-corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. If any subpoenas, investigations, or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

If we or our third-party manufacturers fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We and our third-party manufacturers are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and produce hazardous waste products. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Further, with respect to the operations of our third-party contract manufacturers, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with our products, we could be held liable for any resulting damages, suffer reputational harm or experience a disruption in the manufacture and supply of our product candidates or products.

Risks Related to Employee Matters and Managing Our Operations

We recently completed a substantial reduction in personnel, the effects of which could disrupt our operations. In addition, we may experience difficulties in retaining key employees.

During the year ended December 31, 2017, our workforce was reduced by 122 employees in connection with a reduction in personnel following the failure of our pivotal trials of Fovista as well as natural attrition. Nonetheless, we are continuing to function as a development company and need to continue all or nearly all of our prior business functions to support such development, including clinical operations, regulatory affairs, drug safety, data management, outsourced manufacturing and supply chain, analytical development and quality assurance, as well as all of our general and administrative functions and public company infrastructure. Due to our limited financial resources and the inherent challenges associated with managing such a reduction in personnel, we may not be able to manage effectively the reduction in personnel and transition of operations to remaining employees.

We remain highly dependent on David R. Guyer, M.D., our Executive Chairman, and Glenn P. Sblendorio, our Chief Executive Officer and President, as well as the other principal members of our management, scientific and clinical teams. We do not maintain "key person" insurance for any of our executives or other employees. Although we have entered into letter agreements with our executive officers, each of them and our non-executive employees may terminate their employment with us at any time. As a result, key employees that we expect to retain through specific dates to assist with transition activities may choose not to remain employees. In addition, we may experience difficulties in retaining key employees, given the change in prospects for our company as well as other challenges. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business plan.

Furthermore, replacing any such executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain marketing approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms, if at all, given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development, pipeline expansion and commercialization strategies. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to strategically attract or retain high quality personnel as we implement our new business plan, our ability to pursue our development strategy would be limited.

If we fail to establish and maintain effective internal control over financial reporting, our ability to accurately report our financial results could be adversely affected.

A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements would not be prevented or detected on a timely basis. If any material weakness in our internal control over financial reporting is discovered or occurs in the future, our financial statements may contain material misstatements and we could be required to restate our financial results. As previously disclosed in July 2015, our management concluded that we experienced a material weakness in internal controls related to technical accounting expertise over the accounting for deferred tax assets and income tax accounting in general during certain prior financial reporting periods. The deficiency in the application of our controls relating to technical accounting expertise over the accounting for deferred tax assets and income tax accounting in general resulted in the audit committee of our board of directors concluding that the relevant financial statements should not be relied upon, and our subsequent restatement of the relevant financial statements.

During the year ended December 31, 2015, we took the following steps to remediate the identified material weakness: we added staffing within our finance department and engaged a nationally recognized accounting firm, in each case, with technical expertise in the area of tax accounting and financial reporting. Our management concluded that the identified material weakness in internal control over financial reporting was fully remediated as of December 31, 2015. Although we have remediated this deficiency in internal control over financial reporting, we cannot be certain that the remedial measures that we took in the past or other measures we take in the future, especially in light of our decreased size as a result of the implementation of our reduction in personnel, and the associated decrease in staffing in our accounting and finance areas, will ensure that we maintain adequate controls over our financial reporting going forward and, accordingly, additional material weaknesses could occur or be identified. Any additional material weaknesses or combination of deficiencies could materially

and adversely affect our ability to provide timely and accurate financial information, and the current and future deficiencies may impact investors' confidence in our internal controls and our company, which could cause our stock price to decline.

Risks Related to Information Technology

We rely significantly upon information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cyber security incidents, could harm our ability to operate our business effectively.

In the ordinary course of our business, we and our third-party contractors maintain personal and other sensitive data on our and their respective networks, including our intellectual property and proprietary or confidential business information relating to our business and that of our clinical trial participants and business partners. In particular, we rely on contract research organizations and other third parties to store and manage information from our clinical trials. The secure maintenance of this sensitive information is critical to our business and reputation.

Despite the implementation of security measures, our internal computer systems and those of our third-party contractors are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. In particular, companies and other entities and individuals have been increasingly subject to a wide variety of security incidents, cyber-attacks and other attempts to gain unauthorized access to systems and information. These threats can come from a variety of sources, ranging in sophistication from individual hackers to state-sponsored attacks. Cyber threats may be broadly targeted, or they may be custom-crafted against our information systems or those of our third-party contractors.

For information stored with our third-party contractors, we rely upon, and the integrity and confidentiality of such information is dependent upon, the risk mitigation efforts such third-party contractors have in place. In the recent past, cyber-attacks have become more prevalent and much harder to detect and defend against. Our and our third-party contractors' respective network and storage applications may be subject to unauthorized access by hackers or breached due to operator error, malfeasance or other system disruptions. We might not anticipate or immediately detect such incidents and the damage caused by such incidents. System failures, data breaches and any unauthorized access or disclosure of our information or intellectual property could compromise our intellectual property and expose sensitive business information. System failures or accidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our clinical and commercialization activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy.

A data security breach could also lead to public exposure of personal information of our clinical trial patients and others. Cyber-attacks and the measures we implement to prevent, detect, and respond to them could cause us to incur significant remediation costs, result in product development delays, disrupt key business operations, expose us to contractual damages and/or regulatory liability, divert the attention of our management and key information technology resources, harm our reputation and deter business partners from working with us. Any loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate public disclosure of confidential or proprietary information, we could incur liability and our product research, development and commercialization efforts could be delayed.

Risks Related to Our Common Stock

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and our by-laws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- provide for a classified board of directors such that only one of three classes of directors is elected each year;

- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board of directors;
- provide for advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our certificate of incorporation or by-laws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for stockholders.

Our stock price may be volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their shares of common stock at or above the price at which they purchased their shares. The market price for our common stock may be influenced by many factors, including:

- the success of products or technologies that compete with our product candidates, including results of clinical trials of product candidates of our competitors;
- results of clinical trials for our product candidates and the timing of the receipt of such results;
- the results of our efforts to in-license or acquire the rights to other products, product candidates and technologies for the treatment of ophthalmic diseases;
- political, regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;

- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

For example, following our announcement of initial, top-line results from the first two of our pivotal Fovista trials for the treatment of wet AMD, the closing price of our common stock declined from $38.77 on December 9, 2016 to $5.29 on December 12, 2016 and declined further thereafter. The closing price of our common stock was $2.71 on February 28, 2017. Following periods of volatility in the market price of a company’s stock, securities class-action litigation has often been instituted against that company. We and certain of our current and former executive officers have been named as defendants in purported class action lawsuits following our announcement of the initial, top-line results. See “Part II, Item 1-Legal Proceedings” and “-Risks Related to Our Business Plan, Financial Position and Need for Additional Capital-We and certain of our current and former executive officers have been named as defendants in lawsuits that could result in substantial costs and divert management’s attention.” These proceedings and other similar litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management’s attention and resources, which could seriously harm our business.

If a significant portion of our total outstanding shares are sold into the market, the market price of our common stock could drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Moreover, we have filed registration statements on Form S-8 registering all shares of common stock that we may issue under our equity compensation plans. Once registered on Form S-8, shares underlying these equity awards can be freely sold in the public market upon issuance, subject to volume, notice and manner of sale limitations applicable to affiliates.

We incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, we incur and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish with our periodic Exchange Act reports a report by our management on our internal control over financial reporting. We are also required to include with our annual report an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404, we must document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources and engage outside consultants to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. There is a risk that our internal control over financial reporting may, in the future, be found to be ineffective under Section 404. Our identification of one or more material weaknesses could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be our stockholders’ sole source of gain.

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders’ sole source of gain for the foreseeable future.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our properties consist of office space in New York, New York and Princeton, New Jersey. We lease approximately 13,500 square feet of office space in New York, New York under a lease that terminates in at the end of 2018 and approximately 5,500 square feet of office space in Princeton, New Jersey under a sublease that terminates in March 2020.

Item 3. Legal Proceedings

On January 11, 2017, a putative class action lawsuit was filed against us and certain of our current and former executive officers in the United States District Court for the Southern District of New York, captioned Frank Micholle v. Ophthotech Corporation, et al., No. 1:17-cv-00210. The complaint purports to be brought on behalf of shareholders who purchased our common stock between May 11, 2015 and December 12, 2016. The complaint generally alleges that we and certain of our officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the prospects of our Phase 3 trials for Fovista in combination with anti-VEGF agents for the treatment of wet AMD. The complaint seeks equitable and/or injunctive relief, unspecified damages, attorneys' fees, and other costs.

On March 9, 2017, a second putative class action lawsuit was filed against us and the same group of our current and former executive officers in the United States District Court for the Southern District of New York, captioned Wasson v. Ophthotech Corporation, et al., No. 1:17-cv-01758. The complaint purports to be brought on behalf of shareholders who purchased our common stock between May 11, 2015 and December 9, 2016. The allegations made in the complaint are similar to those made in the Micholle complaint. Putative lead plaintiffs in the Micholle action have moved to consolidate the Micholle and Wasson actions.

On February 7, 2018, a shareholder derivative action was filed against the members of our Board of Directors in the New York Supreme Court Commercial Division, captioned Cano v. Guyer, et al., No. 650601/2018. The complaint alleges that defendants breached their fiduciary duties to our company by adopting a compensation plan that overcompensates the non-employee members of the Board relative to boards of companies of comparable market capitalization and size. The complaint also alleges that defendants were unjustly enriched as a result of the alleged conduct. The complaint purports to seek unspecified damages on our behalf, as well as an order directing us to reform and improve our corporate governance and internal procedures to comply with applicable laws, attorneys' fees, and other costs.

We deny any allegations of wrongdoing and intend to vigorously defend against these lawsuits. We are unable, however, to predict the outcome of these matters at this time. Moreover, any conclusion of these matters in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance would have a material adverse effect on our financial condition and business. In addition, the litigation could adversely impact our reputation and divert management's attention and resources from other priorities, including the execution of business plans and strategies that are important to our ability to grow our business, any of which could have a material adverse effect on our business.

On May 30, 2017, a shareholder derivative action was filed against the members of our Board of Directors in the United States District Court for the Southern District of New York, captioned Etelmendorf v. Bolte, et al., No. 1:17-cv-04042. The complaint alleged that defendants breached their fiduciary duties to our company by causing or permitting the company to make allegedly false and/or misleading statements concerning the prospects of our Phase 3 trials for Fovista in combination with anti-VEGF agents for the treatment of wet AMD, and by approving certain executive compensation. The complaint also alleged that defendants were unjustly enriched as a result of the alleged conduct. The complaint purported to seek unspecified damages on our behalf, as well as an order directing us to reform and comply with our governance obligations, attorneys' fees, and other costs. The defendants moved to dismiss the action in its entirety. Rather than oppose the motion to dismiss, on October 17, 2017, the plaintiff filed a notice of voluntary dismissal without prejudice for this action.

Item 4. Mine Safety Disclosures

None.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuers Purchases of Equity Securities

Our common stock has been publicly traded on The Nasdaq Global Select Market under the symbol "OPHT" since September 25, 2013. The following table sets forth the high and low sale prices per share for our common stock on The Nasdaq Global Select Market for the periods indicated:

	Year ended December 31, 2017		Year ended December 31, 2016	
	High	Low	High	Low
Quarter ended March 31,	$ 5.25	$ 3.24	$ 74.07	$ 40.40
Quarter ended June 30,	$ 3.72	$ 2.24	$ 58.45	$ 41.84
Quarter ended September 30,	$ 3.20	$ 2.31	$ 65.03	$ 46.13
Quarter ended December 31,	$ 3.60	$ 2.25	$ 45.30	$ 4.82

Holders

As of January 31, 2018, there were approximately 102 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

Dividends

We have never declared or paid cash dividends on our common stock, and we do not expect to pay any cash dividends on our common stock in the foreseeable future.

Securities Authorized for Issuance under Equity Compensation Plans

The information required by this item will be set forth in our Proxy Statement for the 2018 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

Recent Sales of Unregistered Securities

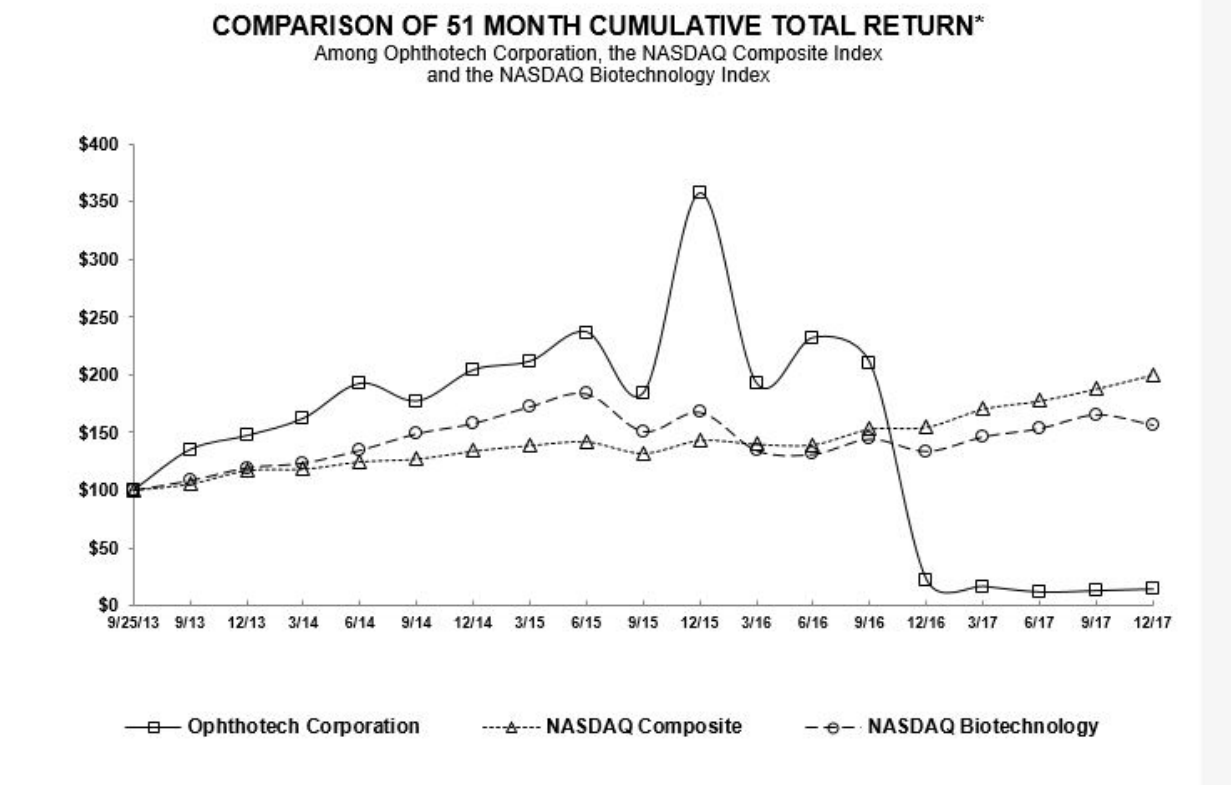
There were no issuances of equity securities that were not registered under the Securities Act of 1933, as amended, or the Securities Act, during the period covered by this Annual Report on Form 10-K.

Purchase of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Stock Performance Graph

The following graph and chart compares the cumulative annual stockholder return on our common stock over the period commencing September 25, 2013 and ending on December 31, 2017, to that of the total return for the NASDAQ Composite Index and the NASDAQ Biotechnology Index, assuming an investment of $100 on August 31, 2013. In calculation cumulative total annual stockholder return, reinvestment of dividends, if any, is assumed. The indices are included for comparative purposes only. They do not necessarily reflect management's opinion that such indices are an appropriate measure of the relative performance of our common stock and are not intended to forecast or be indicative of future performance of our common stock. The following graph and related information shall not be deemed "soliciting material" or to be "filed" with the Securities and Exchange Commission, nor shall such information be incorporated by reference in any of our filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing. We obtained information used on the graph from Research Data Group, Inc., a source we believe to be reliable.



* $100 invested on September 25, 2013 in stock or August 31, 2013 in index, including reinvestment of dividends.

	9/25/2013	9/30/2013	12/31/2013	3/31/2014	6/30/2014	9/30/2014	12/31/2014	3/31/2015
Ophthotech Corporation	$ 100.00	$ 135.05	$ 147.05	$ 162.16	$ 192.32	$ 176.95	$ 203.95	$ 211.50
NASDAQ Composite	100.00	105.46	117.13	118.23	124.11	126.29	133.19	137.78
NASDAQ Biotechnology	100.00	108.52	118.51	122.37	133.81	147.15	156.52	171.61

	6/30/2015	9/30/2015	12/31/2015	3/31/2016	6/30/2016	9/30/2016	12/31/2016	3/31/2017
Ophthotech Corporation	$ 236.64	$ 184.18	$ 356.95	$ 192.14	$ 231.95	$ 209.68	$ 21.95	$ 16.64
NASDAQ Composite	140.65	130.11	141.32	138.82	138.21	151.71	153.66	170.53
NASDAQ Biotechnology	181.93	149.90	166.10	135.14	132.26	145.41	134.22	146.47

	6/30/2017	9/30/2017	12/31/2017
Ophthotech Corporation	$ 11.64	$ 12.82	$ 14.18
NASDAQ Composite	177.58	188.05	200.33
NASDAQ Biotechnology	153.54	166.61	156.63

Item 6. Selected Financial Data

The following selected financial data should be read together with our financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this Annual Report on Form 10-K. We have derived the statements of operations data for the years ended December 31, 2017, 2016, 2015, 2014 and 2013 and the balance sheet data as of December 31, 2017, 2016, 2015, 2014 and 2013 from our audited financial statements, which have been audited by Ernst & Young LLP, an independent registered accounting firm. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period, and our results for any interim period are not necessarily indicative of results to be expected for a full fiscal year.

	Years ended December 31,				
	2017	2016	2015	2014	2013
	(in thousands, except per share data)				
Statements of Operations Data:					
Collaboration revenue	$ 209,977	$ 50,909	$ 51,505	$ 41,259	$ —
Operating expenses:					
Research and development	66,289	196,295	131,012	88,385	33,215
General and administrative	35,683	50,178	44,021	33,387	14,210
Total operating expenses	101,972	246,473	175,033	121,772	47,425
Income (loss) from operations	108,005	(195,564)	(123,528)	(80,513)	(47,425)
Interest income (expense)	1,522	1,704	971	217	(1,454)
Loss on extinguishment of debt	—	—	—	—	(1,091)
Other income (expense)	(34)	34	53	—	(1,175)
Income (loss) before income tax benefit	109,493	(193,826)	(122,504)	(80,296)	(51,145)
Income tax benefit	(4,712)	(406)	(16,787)	36,476	—
Net income (loss)	114,205	(193,420)	(105,717)	(116,772)	(51,145)
Add: accretion of preferred stock dividends	—	—	—	—	(5,891)
Net income (loss) attributable to common stockholders	$ 114,205	$ (193,420)	$ (105,717)	$ (116,772)	$ (57,036)
Net income (loss) per common share:					
Basic	$ 3.18	$ (5.45)	$ (3.06)	$ (3.51)	$ (6.34)
Diluted	$ 3.17	$ (5.45)	$ (3.06)	$ (3.51)	$ (6.34)
Weighted average common shares outstanding:					
Basic	35,919	35,486	34,580	33,258	9,003
Diluted	36,007	35,486	34,580	33,258	9,003

	As of December 31,				
	2017	2016	2015	2014	2013
	(in thousands)				
Balance sheets data:					
Cash, cash equivalents, and marketable securities	$ 166,972	$ 289,278	$ 391,890	$ 463,560	$ 210,596
Total assets	$ 175,576	$ 299,630	$ 428,851	$ 479,786	$ 217,682
Deferred revenue	$ —	$ 209,976	$ 213,066	$ 209,624	$ —
Royalty purchase liability	$ 125,000	$ 125,000	$ 125,000	$ 125,000	$ 41,667
Total liabilities	$ 137,535	$ 394,248	$ 368,904	$ 351,249	$ 47,962
Additional paid-in capital	$ 522,759	$ 504,517	$ 465,927	$ 428,390	$ 352,739
Accumulated deficit	$ (484,754)	$ (598,959)	$ (405,539)	$ (299,822)	$ (183,050)
Total stockholders' equity (deficit)	$ 38,041	$ (94,618)	$ 59,947	$ 128,537	$ 169,720

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of our financial condition and results of operations should be read together with our financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties and should be read together with the "Risk Factors" section of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a science-driven biopharmaceutical company specializing in the development of novel therapies to treat ophthalmic diseases, with a focus on age-related and orphan retinal diseases. Our multi-track strategy is to leverage our clinical experience and retina expertise to develop therapies for large market, age-related retinal diseases, where unmet medical needs remain for these patients, and for orphan eye diseases with a focus on underserved patients, and to utilize a disciplined business development approach to obtain additional products, product candidates and technologies in these disease areas. We believe that there are advantages to pursuing drug development for orphan indications, including the potential for regulatory exclusivity, the potential for clinical trials with smaller sample sizes and the potential for accelerated development timelines. Our team has significant ophthalmic drug development experience and deep relationships with global ophthalmology thought leaders. We have an extensive network of ophthalmic clinical trial sites, having worked with over 250 sites worldwide. We believe that the combination of these factors, together with our experience in designing and executing IND-enabling studies and clinical trials for eye diseases, and specifically back of the eye diseases, provide us a competitive advantage.

We are developing Zimura® (avacincaptad pegol), our complement C5 inhibitor, for dry and wet forms of age-related macular degeneration, or AMD, which is a disorder of the central portion of the retina, known as the macula, that may result in loss of central vision, and autosomal recessive Stargardt disease, or STDG1, which is an orphan inherited retinal disease that also may result in loss of central and peripheral vision. In connection with our Stargardt clinical trial, which we recently initiated, we have expanded our network of thought leaders and clinical trial sites for orphan ophthalmic indications to include leading research university hospitals around the world, where patients with orphan retinal diseases are often referred.

We are actively engaged in extensive business development efforts to identify, evaluate and potentially obtain rights to and develop additional therapeutic and gene therapy product candidates that would complement our strategic goals and leverage our competitive advantages. We believe that our strategy will provide multiple potential opportunities to bring ophthalmic therapies to market.

Zimura

Based on our Zimura development experience to date, as well as scientific literature in the field, we believe there is a strong rationale to pursue the development of our C5 complement inhibitor, Zimura, in multiple ophthalmic diseases. Zimura is a chemically-synthesized, pegylated RNA aptamer. Aptamers are short molecules made up of a single stranded nucleic acid sequence or an amino acid sequence that bind molecular targets with high selectivity and specificity. We have multiple clinical development programs for Zimura ongoing or planned to initiate by the end of 2018. Our ongoing and planned clinical trials for Zimura, all of which are designed to obtain data to guide potential future development efforts, include the following:

- **OPH2003 (geographic atrophy (GA) secondary to dry AMD)**: an ongoing, randomized, double–masked, sham controlled, multi-center Phase 2b clinical trial evaluating the safety and efficacy of Zimura monotherapy in patients with geographic atrophy, or GA, secondary to dry AMD. GA, the end stage of dry AMD, is a disease characterized by retinal cell death and degeneration of retinal tissue.

- **OPH2007 (wet AMD)**: an ongoing, randomized, dose-ranging, open-label, multi-center Phase 2a clinical trial of Zimura in combination with the anti-vascular endothelial growth factor, or anti-VEGF, agent Lucentis® (ranibizumab) for the treatment of wet AMD in patients who have not previously been treated with anti-VEGF agents, referred to as treatment-naïve patients. Wet AMD is characterized by the presence and growth of abnormal new blood vessels under and through the retina.

- **OPH2006 (IPCV)**: an ongoing, randomized, dose-ranging, open-label Phase 2a clinical trial of Zimura in combination with the anti-VEGF agent Eylea® (aflibercept) for the treatment of idiopathic polypoidal choroidal vasculopathy, or IPCV, in patients who have not responded to Eylea monotherapy. IPCV is an age-related retinal

disease involving the choroidal vasculature characterized by the presence of polypoidal lesions, which leads to vision loss. We are at a very early stage of site initiation and patient recruitment for this trial.

- **OPH2005 (autosomal recessive Stargardt disease (STGD1))**: an ongoing, randomized, double-masked, sham controlled, multi-center Phase 2b clinical trial evaluating the safety and efficacy of Zimura monotherapy for the treatment of autosomal recessive Stargardt disease, referred to as STGD1. We are at a very early stage of patient recruitment for this trial.

- **Non-infectious intermediate and posterior uveitis**: a planned open-label Phase 2a clinical trial of Zimura monotherapy for the treatment of non-infectious intermediate and posterior uveitis, a rare inflammatory disease of the back of the eye.

See "Business—Zimura" for additional information regarding each of our ongoing or planned clinical trials.

On-going Business Development and Pipeline Expansion Activities

Since early 2017, we have been engaged in extensive business development efforts. Without limiting any option, the principal focus of this plan, based on our deep expertise and experience in ophthalmic drug development, has been to actively explore obtaining rights to additional products, product candidates and technologies to treat ophthalmic diseases, particularly those in the back of the eye. We evaluated a large number of assets and platforms during 2017 and continue to actively review assets, platforms and other compelling ophthalmology opportunities that would complement our strategic goals. We have considered multiple opportunities over the last several months, including in-licensing, obtaining rights to products, product candidates or technologies, acquisitions, mergers and reverse mergers. Our selection criteria are based on several factors. In general, we are looking for:

- compelling science;

- an identified unmet medical need based on the current standard of care;

- a meaningful commercial opportunity based on existing treatment options and treatment options known to be in development; and

- areas where we believe we can apply our competitive advantages.

Based on our work to date, among the novel technologies we have evaluated, we believe that gene therapy solutions may be particularly well-suited for our strategy as potential treatments for both orphan and age-related eye diseases. We remain committed to being opportunistic and will consider other compelling opportunities that may emerge.

Gene Therapy Research Programs

In February 2018, we announced that an element of our strategy will include initiating collaborative gene therapy programs focused on discovering and developing novel gene therapy technologies to treat retinal diseases. We intend to investigate promising gene therapy product candidates through collaborations with leading companies and academic and research institutions in the United States and internationally.

For our first gene therapy research collaboration, we have entered into a series of sponsored research agreements with the University of Massachusetts Medical School, or UMMS, and its Horae Gene Therapy Center to utilize their novel gene delivery technologies and "minigene" therapy approach to target retinal diseases. AAV vectors are generally limited as a delivery vehicle by the size of their genetic cargo, which is restricted to approximately 4,700 base pairs of genetic code. The use of "minigenes" as a novel therapeutic strategy seeks to deliver a shortened but still functional form of a larger gene packaged into a standard-size AAV delivery vector. The "minigene" strategy may offer an innovative solution for diseases that would otherwise be difficult to address through conventional AAV gene replacement therapy where the size of the gene of interest exceeds the transgene packaging capacity of conventional AAV vectors. Furthermore, one of the differentiating advantages of the "minigene" approach is that it could potentially provide a treatment that is independent of the specific mutation a patient has. The scope of the UMMS collaboration addresses Leber Congenital Amaurosis type 10, or LCA10, which is the most common type of LCA and is caused by mutations in the CEP290 gene, and STDG1, which is caused by mutations in the ABCA4 gene. LCA10 and STDG1 are both orphan inherited degenerative retinal diseases that lead to vision loss without any FDA or EMA approved treatment. As a condition of each sponsored research agreement, UMMS has granted

us an option to obtain an exclusive license to any patents or patent applications that result from the sponsored research. Our aggregate financial commitment for the sponsored research agreements is in the low, single-digit millions of dollars.

Remaining Fovista Activities

In December 2016 and August 2017, we received initial top-line data from our three pivotal clinical trials, referred to as OPH1002, OPH1003 and OPH1004, evaluating the anti-platelet derived growth factor, or anti-PDGF, aptamer Fovista® (pegpleranib) administered in combination with anti-VEGF agents for the treatment of wet AMD, indicating that these trials failed to achieve their pre-specified primary endpoints. We have terminated these trials, as well as several other smaller Fovista trials in wet AMD, which we have referred to as the Fovista Expansion Studies. The National Eye Institute and an academic pre-clinical program are evaluating various uses of Fovista for the treatment of retinal capillary hemangiomas associated with the orphan disease Von-Hippel-Lindau Syndrome, and for the treatment of retinoblastoma, a rare cancer of the eye in children, respectively. We have completed our commitments to these two programs, which primarily involved providing Fovista drug product and drug substance that we had on hand for use in the studies.

Therefore, we do not currently expect any development activity for Fovista going forward, as we have no intentions to resume development of Fovista in wet AMD and our supply commitments for the two external studies are complete.

Novartis Agreement

In May 2014, we entered into a licensing and commercialization agreement with Novartis Pharma AG, or Novartis, which we refer to as the Novartis Agreement. Under the Novartis Agreement, we granted Novartis exclusive rights under specified patent rights, know-how and trademarks controlled by us to manufacture, from bulk active pharmaceutical ingredient, or API, supplied by us, standalone Fovista products and products combining Fovista with an anti-VEGF agent to which Novartis has rights in a co-formulated product, for the treatment, prevention, cure or control of any human disease, disorder or condition of the eye, and to develop and commercialize those licensed products in all countries outside of the United States, which we refer to as the Novartis Territory. We agreed to use commercially reasonable efforts to complete our pivotal Phase 3 clinical program for Fovista and Novartis agreed to use commercially reasonable efforts to develop a standalone Fovista product and a co-formulated product containing Fovista and an anti-VEGF agent to which Novartis has rights, as well as a pre-filled syringe presentation of such products and to use commercially reasonable efforts, subject to obtaining marketing approval, to commercialize licensed products in the Novartis Territory in accordance with agreed development and marketing plans. Novartis paid us a $200.0 million upfront fee upon execution of the Novartis Agreement, as well as $50.0 million upon the achievement of each of two patient enrollment-based milestones, and $30.0 million upon the achievement of a third, and final, enrollment-based milestone, for an aggregate of $330.0 million. In July 2017, we and Novartis entered into a letter agreement to streamline the process and timeline for evaluating data from the final Fovista Phase 3 clinical trial once it became available. On October 23, 2017, following the failure of the Phase 3 Fovista program and pursuant to the terms of the July 2017 letter agreement, Novartis elected to terminate the Novartis Agreement with immediate effect.

Financial matters

As of December 31, 2017, we had cash, cash equivalents and marketable securities of $167.0 million, of which approximately $2.0 million is committed to satisfying our remaining financial obligations with respect to the wind-down of the Fovista Phase 3 trials and obligations incurred in connection with our reduction in personnel, which was substantially completed during 2017. For 2018, we expect the cash required to fund our operations and capital expenditures, including our Zimura development programs and collaborative gene therapy research programs, as currently planned will range between $50.0 million and $55.0 million.

As a result of our ongoing reassessment of our development programs and potential business development opportunities and pipeline expansion activities, we may modify, expand or terminate some or all of our research or development programs or clinical trials at any time. The outcome of these reassessments, as well as the progress of our plans to potentially acquire additional products, product candidates or technologies will determine whether and to what extent we will continue to incur research and development costs for each of our development programs going forward.

Our ability to become and remain profitable depends on our ability to generate revenue in excess of our expenses. We do not expect to generate significant product revenue unless, and until, we obtain marketing approval for, and commercialize, any of our product candidates, which, if we are successful, will likely take at least several years. We may be unsuccessful in our efforts to develop and commercialize these product candidates. Even if we succeed in developing and commercializing one or more of our product candidates, we may never achieve sufficient sales revenue to achieve or maintain

profitability. Our capital requirements will also depend on many other factors, including whether we are successful in our pursuit to acquire or in-license and subsequently develop additional product candidates or technologies. We may need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

Financial Operations Overview

Revenue

In May 2014, we entered into the Novartis Agreement, which is described below under "—Liquidity and Capital Resources—Licensing and Commercialization Agreement with Novartis Pharma AG." We used the relative selling price method to allocate arrangement consideration to our performance obligations under the Novartis Agreement. Upon entry into the Novartis Agreement, we received an upfront payment of $200.0 million, which was not previously recorded as revenue due to our right to terminate the agreement in the event that the parties were prevented from materially progressing the development or commercialization of Fovista products for a specified period as a result of specified governmental actions and the associated termination fee equivalent to the entire $200.0 million upfront payment, which we would have been required to pay if we elected to exercise this termination option. In each of September 2014 and March 2015, we achieved a $50.0 million enrollment-based milestone, and in June 2016, we achieved a $30.0 million enrollment-based milestone, for an aggregate total of $130.0 million, under the Novartis Agreement. In July 2017, we entered into a letter agreement with Novartis, which resulted in the recognition of the remaining deferred revenue under the Novartis Agreement during the third quarter of 2017, as described below under "Critical Accounting Policies and Significant Judgments and Estimates—Revenue Recognition—Collaboration Revenue". The recognition of this revenue during the period did not impact our cash balance. Below is a summary of the components of our collaboration revenue for the years ended December 31, 2017, 2016 and 2015:

	Years ended December 31,		
	2017	2016	2015
	(in thousands)		
License revenue	$ 152,912	$ 22,937	$ 38,083
Research and development activity revenue	56,180	9,741	8,378
API transfer revenue	754	18,212	5,020
Joint operating committee revenue	131	19	24
Total collaboration revenue	$ 209,977	$ 50,909	$ 51,505

On October 23, 2017, following the failure of the Fovista Phase 3 program and pursuant to the terms of the July 2017 letter agreement, Novartis elected to terminate the Novartis Agreement with immediate effect. As we have no products approved for sale, we will not receive any revenue from any product candidates that we develop until we obtain regulatory approval and commercialize such products, or until we potentially enter into agreements with third parties for the development and commercialization of product candidates. If our development efforts for any of our product candidates result in regulatory approval or we enter into collaboration agreements with third parties, we may generate revenue from product sales or from such third parties.

Research and Development Expenses

Research and development expenses primarily consist of costs associated with the development and clinical testing and manufacturing of Zimura and, historically, Fovista, as well as costs associated with the preclinical development of other product candidates and formulations. Our research and development expenses consist of:

- external research and development expenses incurred under arrangements with third parties, such as contract research organizations, or CROs, and other vendors and contract manufacturing organizations, or CMOs, for the production of API and drug product; and
- employee-related expenses, including salaries, benefits and share-based compensation expense.

Research and development expenses also include costs of acquired product licenses and related technology rights where there is no alternative future use, costs of prototypes used in research and development, consultant fees and amounts paid to collaborative partners. We expect that research and development expenses in the future will also include the costs of our

collaborative gene therapy research programs, including the costs of our research collaboration with UMMS, entered into in February 2018.

All research and development expenses are charged to operations as incurred in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic, or ASC, 730, *Research and Development*. We account for non-refundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received, rather than when the payment is made. To date, the large majority of our research and development activity has been related to Fovista and Zimura. We do not currently utilize a formal time allocation system to capture expenses on a project-by-project basis because we record expenses by functional department. Accordingly, we do not allocate expenses to individual projects or product candidates, although we do allocate some portion of our research and development expenses by functional area and by compound, as shown below.

The following table summarizes our research and development expenses for the years ended December 31, 2017, 2016 and 2015:

	Years ended December 31,		
	2017	2016	2015
	(in thousands)		
Fovista	$ 21,698	$ 129,661	$ 86,906
Zimura	11,986	7,400	7,644
Personnel-related	19,413	26,700	15,830
Share-based compensation	11,114	21,380	16,608
Other	2,078	11,154	4,024
	$ 66,289	$ 196,295	$ 131,012

We expect to continue to incur significant research and development expenses as we pursue the development of Zimura as currently planned. We also expect very limited research and development expenses related to Fovista in the future, as we have terminated our Fovista development programs and have no plans for the future development of Fovista. As we pursue our ongoing and planned Zimura development programs, or as we commence any new development efforts in relation to additional product candidates we may in-license or acquire as we pursue our business plan, we expect that our overall research and development expenses will begin to increase from the current level of expenditure.

Our expenses may exceed our expectations if we experience delays in enrollment or with the availability of drug supply for our clinical trials, if we experience any unforeseen issue in our ongoing clinical trials or if we further expand the scope of our collaborative research programs or clinical trials. Our costs may also exceed our expectations for other reasons, for example, if we experience issues with process development, establishing or scaling-up of manufacturing activities or activities to enable and qualify second source suppliers or if we decide to increase licensing or preclinical research and development activities, including by building internal capabilities or pursuing internal research efforts.

The future development of our product candidates is highly uncertain. We expect the clinical development for Zimura will continue for at least the next several years. At this time, we cannot reasonably estimate the remaining costs necessary to complete clinical development, to complete process development and manufacturing scale-up and validation activities or to potentially seek marketing approval with respect to our product candidates.

The successful development of our product candidates is subject to numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress and expense of our research and development activities;
- the potential benefits of our product candidates over other therapies;
- clinical trial results;
- the terms and timing of regulatory approvals;
- our ability to market, commercialize and achieve market acceptance for any of our product candidates; and

- our ability to successfully file, prosecute, defend and enforce patent claims and other intellectual property rights, together with associated expenses.

A change in the outcome of any of these variables with respect to the development of our product candidates could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if regulatory authorities were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate or if we experience significant delays in enrollment in any clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

See the "Liquidity and Capital Resources" section on page 92 of this Annual Report on Form 10-K for more information regarding our current and future financial resources and our expectations regarding our research and development expenses and funding requirements.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for personnel, including share-based compensation expense, in our executive, legal, finance, human resources, investor relations and business development functions. Other general and administrative expenses include facility costs and professional fees for legal, patent, pre-launch commercialization activities, travel expenses, consulting and accounting services.

We anticipate that our general and administrative expenses will decrease in future periods as a result of a reduction in personnel to focus on our revised business plan, which we expect will involve a total expected workforce of approximately 40 employees. We substantially completed the reduction in personnel during 2017 as part of implementing our revised business plan.

Interest Income

Our cash, cash equivalents and marketable securities are invested primarily in money market funds, U.S. Treasury securities and investment-grade corporate debt securities, which generate a nominal amount of interest income.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued research and development expenses, revenue recognition, share-based compensation and income taxes described in greater detail below. We base our estimates on our limited historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies are described in more detail in the notes to our financial statements appearing elsewhere in this Annual Report on Form 10-K. Of those policies, we believe that the following accounting policies are the most critical to aid our stockholders in fully understanding and evaluating our financial condition and results of operations.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses are related to expenses incurred with respect to CROs, CMOs and other vendors in connection with research and development and manufacturing activities.

We base our expenses related to CROs and CMOs on our estimates of the services received and efforts expended pursuant to quotations and contracts with such vendors that conduct research and development and manufacturing activities on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the applicable research and development or manufacturing expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in us reporting amounts that are too high or too low in any particular period. There have been no material changes in estimates for the periods presented.

Revenue Recognition—Collaboration Revenue

In May 2014, we received an upfront payment of $200.0 million in connection with our entry into the Novartis Agreement, which was not recorded as revenue due to the existence of a contingency with respect to our right to terminate the agreement in certain circumstances and the associated termination fee equivalent to the entire $200.0 million upfront payment, which we would have been required to pay if we elected to exercise this termination option. In each of September 2014 and March 2015, we achieved a $50.0 million enrollment-based milestone, and in June 2016, we achieved a $30.0 million enrollment-based milestone, for an aggregate total of $130.0 million in milestones, under the Novartis Agreement. We used the relative selling price method to allocate these payments to contract deliverables based on our performance obligations under the Novartis Agreement.

The July 2017 letter agreement with Novartis resolved the contingency with respect to our termination right, allowing us to immediately recognize as revenue the portion of the upfront payment allocated using the relative selling price method to deliverables completed during prior periods. During the third quarter of 2017, we completed the remaining deliverables under the Novartis Agreement and the July 2017 letter agreement and recognized as revenue the balance of all of the payments previously received from Novartis related to licensing, research and development, manufacturing and joint operating committee activities that had been previously deferred using the relative selling price method. In total, during the third quarter of 2017, we recognized $206.7 million in previously deferred collaboration revenue in connection with the Novartis Agreement. The recognition of this revenue during the period did not impact our cash balance. On October 23, 2017, following the failure of the Fovista Phase 3 program and pursuant to the terms of the July 2017 letter agreement, Novartis elected to terminate the Novartis Agreement with immediate effect.

Below is a summary of the components of our collaboration revenue for the years ended December 31, 2017, 2016 and 2015:

	Years ended December 31,		
	2017	2016	2015
	(in thousands)		
License revenue	$ 152,912	$ 22,937	$ 38,083
Research and development activity revenue	56,180	9,741	8,378
API transfer revenue	754	18,212	5,020
Joint operating committee revenue	131	19	24
Total collaboration revenue	$ 209,977	$ 50,909	$ 51,505

Royalty Purchase Liability

The proceeds from the financing we received under our Fovista royalty financing agreement with Novo A/S, or the Novo Agreement, have been recorded as a liability on our Balance Sheet in accordance with ASC 730, *Research and Development*. Although there is no explicit repayment obligation contained in the Novo Agreement, because there was a significant related party relationship between us and Novo A/S at the time the Novo Agreement was entered into, we are treating our obligation to make royalty payments under the Novo Agreement as an implicit obligation to repay the funds advanced by Novo A/S, and thus have recorded the proceeds as a liability on our Balance Sheet. In the event that we make royalty payments to Novo A/S, we will reduce the liability balance. At the time that such royalty payments become probable and estimable, and if such amounts exceed the liability balance, we will impute interest accordingly on a prospective basis based on such estimates, which would result in a corresponding increase in the liability balance.

Share-Based Compensation

We account for all share-based compensation payments issued to employees, non-employee directors, and consultants by estimating the fair value of each equity award. Accordingly, share-based compensation expense is measured based on the estimated fair value of the awards on the date of grant, net of forfeitures. We recognize compensation expense for the portion of the award that is ultimately expected to vest over the period during which the recipient renders the required services to us on a straight-line basis. In accordance with authoritative guidance, we re-measure the fair value of consultant share-based awards as the awards vest, and recognize the resulting value, if any, as expense during the period the related services are rendered.

We apply the fair value recognition provisions of ASC 718, *Compensation—Stock Compensation*. Determining the amount of share-based compensation to be recorded requires us to develop estimates of the fair value of stock options as of their grant date. We recognize share-based compensation expense ratably over the requisite service period, which in most cases is the vesting period of the award. For grants containing performance-based vesting provisions, expense is recognized over the estimated achievement period. Calculating the fair value of share-based awards requires that we make highly subjective assumptions.

We use the Black-Scholes option pricing model to value our stock option awards and the options to purchase shares under our employee stock purchase plan. Use of this valuation methodology requires that we make assumptions as to the volatility of our common stock, the expected term of our stock options, and the risk-free interest rate for a period that approximates the expected term of our stock options and the expected dividend yield of our common stock. As a recent public company, we do not have sufficient history to estimate the volatility of our common stock price or the expected life of the options. We calculate expected volatility based on reported data for similar publicly traded companies for which historical information is available and will continue to do so until the historical volatility of our common stock is sufficient to measure expected volatility for future option grants.

We use the simplified method as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term of stock option grants to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no current intention to pay cash dividends. The weighted-average assumptions used to estimate grant date fair value of stock options using the Black-Scholes option pricing model were as follows for the years ended December 31, 2017, 2016 and 2015:

	Years ended December 31,		
	2017	**2016**	**2015**
Expected common stock price volatility	81%	71%	72%
Risk-free interest rate	1.82% - 2.38%	1.14% - 2.37%	1.35% - 2.24%
Expected term of options (years)	6.1	6.1	6.2
Expected dividend yield	—	—	—

We estimate the fair value of restricted stock units, or RSUs, granted to employees using the closing market price of our common stock on the date of grant.

We also estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from our estimates. We use historical data to estimate pre-vesting forfeitures and record share-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised.

Share-based compensation expense for equity grants to employees, non-employee directors and consultants was $18.2 million, $31.7 million and $24.8 million for the years ended December 31, 2017, 2016, and 2015, respectively. As of December 31, 2017, we had $20.7 million of total unrecognized share-based compensation expense, which we expect to recognize over a weighted-average remaining vesting period of approximately 2.4 years. We expect our share-based compensation expense for our equity awards to employees, non-employee directors and consultants to increase as a result of recognizing our existing unrecognized share-based compensation for awards that will vest and as we issue additional equity awards to attract and retain our employees.

For the years ended December 31, 2017, 2016 and 2015, we allocated share-based compensation as follows:

	Years ended December 31,		
	2017	2016	2015
	(in thousands)		
Research and development	$ 11,114	$ 21,380	$ 16,608
General and administrative	7,057	10,280	8,152
Total	$ 18,171	$ 31,660	$ 24,760

Income Taxes

On December 22, 2017, the U.S. Tax Cuts and Jobs Act, or the TCJA, was enacted reducing the corporate tax rate from 35% to 21% effective for tax years beginning on or after January 1, 2018. As a result of the passage of the TCJA, the value of our deferred tax assets and related valuation allowance was reduced by a provisional amount of approximately $54.6 million. Additionally, under the TCJA, the Corporate Alternative Minimum Tax, or AMT, was repealed. Accordingly, our previously recorded AMT credits of approximately $3.5 million are now refundable over a four-year period beginning in 2018 and the previously recorded valuation allowance for these AMT credits has been reversed as a result of the TCJA during the fourth quarter of 2017.

The deferred tax assets associated with our losses incurred to date in 2017 have a full valuation allowance recorded against them due to our history of losses and the lack of other positive evidence to support future taxable income against which these losses could be applied. See Note 8 to our financial statements in Part IV-Item 15 of this Annual Report on Form 10-K for further information regarding our expectations with respect to our income tax provision.

We are projecting a tax loss for 2017, none of which may be carried back to any prior taxable years. Although we recognized income under U.S. generally accepted accounting principles, or GAAP, during 2017, this income is primarily due to the recognition of deferred income that had previously been recorded on our federal and state income tax returns. This recognition of income resulted in the reduction of a deferred tax asset that was completely offset by a previously recorded valuation allowance. With respect to the remaining deferred tax assets, except for the AMT credits previously discussed above, there was no change in the amount of assets realizable at December 31, 2017.

Results of Operations

Comparison of Years Ended December 31, 2017 and 2016

	Years ended December 31,		Increase (Decrease)
	2017	2016	
	(in thousands)		
Statements of Operations Data:			
Collaboration revenue	$ 209,977	$ 50,909	$ 159,068
Operating expenses:			
Research and development	66,289	196,295	(130,006)
General and administrative	35,683	50,178	(14,495)
Total operating expenses	101,972	246,473	(144,501)
Income (loss) from operations	108,005	(195,564)	(303,569)
Interest income	1,522	1,704	(182)
Other income (expense)	(34)	34	(68)
Income (loss) before income tax benefit	109,493	(193,826)	(303,319)
Income tax benefit	(4,712)	(406)	(4,306)
Net income (loss)	$ 114,205	$ (193,420)	$ (307,625)

Collaboration Revenue

Collaboration revenue for the year ended December 31, 2017 was $210.0 million, an increase of $159.1 million compared to $50.9 million for the year ended December 31, 2016. Collaboration revenue for the year ended December 31, 2017 increased as we completed all deliverables required under the Novartis Agreement during the period. The July 2017 letter

agreement with Novartis resolved the contingency with respect to our right to terminate the agreement in the event that the parties were prevented from materially progressing the development or commercialization of Fovista products for a specified period as a result of specified governmental actions and the associated termination fee equivalent to the entire $200.0 million upfront payment, which we would have been required to pay if we elected to exercise this termination option. We had previously deferred the entire $200.0 million upfront payment based on this contingency. As a result of our entry into the letter agreement and resolution of the contingency, we immediately recognized the revenue attributable to deliverables completed during prior periods. Further, as our remaining deliverables under the Novartis Agreement and the letter agreement were completed during the third quarter of 2017, we recognized all of the remaining collaboration revenue previously deferred under the Novartis Agreement. Using the relative selling price method, we recognized $152.9 million related to the license we delivered to Novartis under the Novartis Agreement, $56.2 million related to the research and development activities we performed under the Novartis Agreement, $0.8 million related to Fovista API we previously transferred to Novartis, and $0.1 million related to our joint operating committee participation obligations.

Collaboration revenue for the year ended December 31, 2016 was $50.9 million, of which $22.9 million was allocated to the license delivered to Novartis under the Novartis Agreement, $9.7 million was allocated to research and development activities performed under the Novartis Agreement, $18.2 million related to Fovista API we transferred to Novartis, and a de minimis amount of revenue was associated with our joint operating committee participation obligation during the same period.

Research and Development Expenses

Our research and development expenses were $66.3 million for the year ended December 31, 2017, a decrease of $130.0 million compared to $196.3 million for the year ended December 31, 2016. Research and development expenses for the year ended December 31, 2017 include approximately $7.5 million in costs related to our previously announced reduction in personnel. The decrease in research and development expenses for the year ended December 31, 2017 was primarily due to a $107.1 million decrease in costs associated with our Fovista program, including our Fovista Phase 3 clinical program and our Fovista Expansion Studies, a $6.2 million decrease in professional services and consulting fees, and a $10.3 million decrease in share-based compensation costs. The decreased costs for our Fovista program included lower costs related to Fovista manufacturing activities and lower clinical trial costs as a result of the wind-down of OPH1002 and OPH1003 and the Fovista Expansion Studies. This overall decrease was offset by a $4.6 million increase associated with our Zimura program, primarily related to manufacturing expenses.

General and Administrative Expenses

Our general and administrative expenses were $35.7 million for the year ended December 31, 2017, a decrease of $14.5 million, compared to $50.2 million for the year ended December 31, 2016. General and administrative expenses for the year ended December 31, 2017 include approximately $5.6 million in costs related to our previously announced reduction in force and the termination of facilities leases. The decrease in general and administrative expenses was primarily due to a decrease in costs to support our operations and infrastructure offset by the additional severance and lease termination costs.

Interest Income

Interest income for the year ended December 31, 2017 was $1.5 million compared to interest income of $1.7 million for the year ended December 31, 2016. The decrease in interest income earned during the year ended December 31, 2017 was the result of a decrease in our cash and cash equivalent balances available for investment.

Income Tax Benefit

During the year ended December 31, 2017, we recorded a benefit from income taxes of approximately $4.7 million, which primarily related to a $3.5 million reduction in our valuation allowances for AMT credits to reflect the impact of the TCJA enactment and a settlement of a franchise tax audit for $1.4 million partially offset by the reversal of previously recoded benefits related to the change in unrealized gains of our investment portfolio. Although we had $109.5 million of net income before income taxes for the year ended December 31, 2017 as a result of the recognition of deferred revenue under the Novartis Agreement, we expect a net loss for tax purposes for 2017 with minimal taxes due. For tax purposes, we treated payments received under the Novartis Agreement as revenue at the time the payments were received and the related deferred tax assets had a full valuation recorded against them.

During the year ended December 31, 2016, we recorded a benefit from income taxes of approximately $0.4 million, which related to unanticipated refunds received and the reduction in our valuation allowances to reflect the income tax associated with unrealized gains in our investment portfolio.

Comparison of Years Ended December 31, 2016 and 2015

	Years ended December 31,		Increase (Decrease)
	2016	2015	
	(in thousands)		
Statements of Operations Data:			
Collaboration revenue	$ 50,909	$ 51,505	$ (596)
Operating expenses:			
Research and development	196,295	131,012	65,283
General and administrative	50,178	44,021	6,157
Total operating expenses	246,473	175,033	71,440
Loss from operations	(195,564)	(123,528)	72,036
Interest income	1,704	971	733
Other income	34	53	(19)
Loss before income tax provision	(193,826)	(122,504)	71,322
Income tax benefit	(406)	(16,787)	(16,381)
Net loss	$ (193,420)	$ (105,717)	$ 87,703

Collaboration Revenue

Collaboration revenue for the year ended December 31, 2016 was approximately $50.9 million. Using the relative selling price method, we allocated $22.9 million to the license delivered to Novartis under the Novartis Agreement, $9.7 million to research and development activities performed under the Novartis Agreement, $18.2 million related to the Fovista API we transferred to Novartis, and a de minimis amount of revenue associated with our joint operating committee participation obligation during the year ended December 31, 2016.

Collaboration revenue for the year ended December 31, 2015 was $51.5 million, of which $38.1 million was allocated to the license delivered to Novartis under the Novartis Agreement, $8.4 million was allocated to research and development activities performed under the Novartis Agreement and $5.0 million related to Fovista API we transferred to Novartis during the same period.

Research and Development Expenses

Our research and development expenses were $196.3 million for the year ended December 31, 2016, an increase of $65.3 million compared to $131.0 million for the year ended December 31, 2015. The increase in research and development expenses for the year ended December 31, 2016 was primarily due to a $42.8 million increase in costs associated with our Fovista program, including our Fovista Phase 3 clinical program and our Fovista Expansion Studies. The increased costs for our Fovista program included higher clinical trial costs relating to increased patient enrollment in the Fovista Phase 3 clinical trials and the Fovista Expansion Studies, the initiation of additional Fovista Expansion Studies, as well as higher manufacturing costs to support our clinical trials and for API validation activities, and certain costs related to the cancellation of Fovista API purchase orders following our receipt of initial, top-line data from OPH1002 and OPH1003 in December 2016. Also contributing to the overall increase was a $10.9 million increase to personnel expenses associated with additional research and development staffing and a $4.8 million increase to share-based compensation costs. In addition, costs related to professional services and consulting fees increased by $6.1 million.

General and Administrative Expenses

Our general and administrative expenses for the year ended December 31, 2016 were $50.2 million, an increase of $6.2 million, compared to $44.0 million for the year ended December 31, 2015. The increase was primarily due to an increase in personnel expenses of $2.6 million, including $2.1 million in share-based compensation costs, an increase of $2.8 million in facility costs, as well as other costs to support the expansion of our operations during 2016, including our public company infrastructure, and the early stages of a commercial organization. Also contributing to the increase were increased costs for professional services and consulting fees of $0.8 million.

Interest Income

Interest income for the year ended December 31, 2016 was $1.7 million compared to net interest expense of $1.0 million for the year ended December 31, 2015. The increase in interest income earned during the year ended December 31, 2016 was the result of an increase in our average investment portfolio balances, and a change in the mix of our investment portfolio, which previously included only investments in U.S. Treasury securities and now includes investments in certain investment-grade corporate debt securities.

Income Tax Benefit

During the year ended December 31, 2016, we recorded a benefit from income taxes of approximately $0.4 million, which related to unanticipated refunds received and the reduction in our valuation allowances to reflect the income tax associated with unrealized gains in our investment portfolio. During the year ended December 31, 2015, we recorded a benefit for income taxes of approximately $16.8 million, which related to our tax losses for tax year 2015 and our ability to carry these losses back to 2014 to recapture a portion of the federal income tax payments we paid in 2014.

Liquidity and Capital Resources

Sources of Liquidity

Since inception, we have financed our operations primarily through private placements of our preferred stock, venture debt borrowings, funding we received under the Novo Agreement, our initial public offering of common stock, which we closed in September 2013, our follow-on public offering of common stock, which we closed in February 2014, and funds we received under the Novartis Agreement. In September 2013, we issued and sold an aggregate of 8,740,000 shares of common stock in our initial public offering at a public offering price of $22.00 per share. We received net proceeds from the initial public offering of $175.6 million. In February 2014, we issued and sold 1,900,000 shares of common stock and selling shareholders sold 728,571 shares of common stock in a follow-on public offering at a public offering price of $31.50 per share. We received net proceeds of $55.4 million from the follow-on offering. The Novo Agreement, which is described in more detail below, provided for financing of up to $125.0 million in the aggregate in return for the sale to Novo A/S of royalty interests in worldwide sales of Fovista. We received an aggregate of $125.0 million from this financing in separate tranches in May 2013, January 2014 and November 2014, which constitutes the full amount of funding under the Novo Agreement. In May 2013, we issued and sold an aggregate of 6,666,667 shares of our series C preferred stock at a price per share of $2.50, for an aggregate purchase price of $16.7 million. In August 2013, we issued and sold an aggregate of 13,333,333 additional shares of our series C preferred stock to the same purchasers at a price per share of $2.50, for an aggregate purchase price of $33.3 million.

In May 2014, we received an upfront payment of $200.0 million upon execution of the Novartis Agreement in connection with the grant of a license for the rights to commercialize Fovista outside the United States. In each of November 2014 and April 2015 we received payments of $50.0 million upon the achievement of two patient enrollment-based milestones, and in August 2016, $30.0 million upon the achievement of a third, and final, enrollment-based milestone, for an aggregate total of $130.0 million. In connection with the receipt of the upfront payment from Novartis, we made a milestone payment in June 2014 of approximately $19.8 million to Nektar Therapeutics, or Nektar, pursuant to a license, manufacturing and supply agreement that we agreed to terminate with Nektar in October 2017.

Cash Flows

As of December 31, 2017, we had cash, cash equivalents and marketable securities totaling $167.0 million and no debt. We primarily invest our cash, cash equivalents and marketable securities in U.S. Treasury securities, money market funds and certain investment-grade corporate debt securities.

The following table shows a summary of our cash flows for the years ended December 31, 2017, 2016 and 2015:

	Years ended December 31,		
	2017	2016	2015
	(in thousands)		
Net cash (used in) provided by:			
Operating Activities	$ (121,821)	$ (108,596)	$ (78,531)
Investing Activities	154,792	13,731	247,803
Financing Activities	71	6,934	12,775
Net change in cash and cash equivalents	$ 33,042	$ (87,931)	$ 182,047

Cash Flows from Operating Activities

Net cash used in operating activities for the year ended December 31, 2017 was $121.8 million and relates primarily to net cash used for the wind-down of OPH1002 and OPH1003 and the Fovista Expansion Studies, implementation of a previously announced reduction in personnel and related costs, and cancellation fees related to manufacturing commitments, as well as continuation of our OPH1004 trial through initial, top-line data in August 2017 and wind-down thereafter and general and administrative and corporate infrastructure expense.

Net cash used in operating activities for the year ended December 31, 2016 was $108.6 million and related primarily to net cash used to fund our Fovista Phase 3 program, our Fovista Expansion Studies, Fovista manufacturing activities, as well as manufacturing and clinical trial costs for our Zimura program and expenditures related to general and administrative expenses.

See "—Funding Requirements" below for a description of how we expect to use our cash for operating activities in future periods.

Cash Flows from Investing Activities

Net cash provided by investing activities for the year ended December 31, 2017 was $154.8 million and relates primarily to proceeds from the maturities of marketable securities totaling $166.8 million offset by purchases of marketable securities totaling $12.0 million. Net cash provided by investing activities for the year ended December 31, 2016 was $13.7 million and relates primarily to proceeds from the maturity of marketable securities totaling $86.5 million offset by purchases of marketable securities totaling $72.2 million.

Cash Flows from Financing Activities

Net cash provided by financing activities was $0.1 million for the year ended December 31, 2017 and $6.9 million for the year ended December 31, 2016 and related to the proceeds from stock option plan exercises and purchases made under our employee stock purchase plan.

Funding Requirements

Our product candidate Zimura is in clinical development. We expect to continue to incur significant research and development expenses as we pursue the development of Zimura as currently planned. We could also incur additional research and development expenses if we conclude that there is a scientific rationale for potentially developing, or if we undertake the development of Zimura in additional indications, beyond those already in development, and as we evaluate and potentially in-license or acquire, and undertake development of, additional product candidates, including any promising product candidates that emerge from our collaborative gene therapy research programs. Furthermore, if we successfully develop and obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. We are party to an agreement with Archemix that imposes significant milestone payment obligations on us in connection with our achievement of specific clinical, regulatory and commercial milestones with respect to Zimura. It is likely that any future in-licensing or acquisition agreements that we enter into with respect to additional products, product candidates or technologies would include similar obligations.

We expect that we will continue to incur significant expenses as we:

- continue the clinical development of Zimura as currently planned or potentially in other indications if we believe there is a sufficient scientific rationale to pursue such development;
- in-license or acquire the rights to, and pursue the development of, other products, product candidates or technologies;
- pursue our collaborative gene therapy research programs;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing, quality control, quality assurance and scientific personnel, especially if we are successful in acquiring or in-licensing rights to additional products, product candidates or technologies or progressing the clinical development of any of our product candidates or if we decide to establish internal gene therapy capabilities;
- seek marketing approval for any product candidates that successfully complete clinical trials;

- expand our outsourced manufacturing activities or establish commercial operations or sales, marketing and distribution capabilities, if we receive, or expect to receive, marketing approval for any of our product candidates; and

- expand our general and administrative functions to support future growth of the company.

As of December 31, 2017, we had cash, cash equivalents and marketable securities of $167.0 million, of which approximately $2.0 million is committed to satisfying our remaining financial obligations with respect to the wind-down of the Fovista Phase 3 trials and obligations incurred in connection with our reduction in personnel substantially completed during 2017. For 2018, we expect the cash required to fund our operations and capital expenditures, including our Zimura development programs and collaborative gene therapy research programs, as currently planned will range between $50.0 million and $55.0 million. We also had $137.5 million in total liabilities as of December 31, 2017, of which $125.0 million related to the Novo Agreement, which we are required to show as a liability on our balance sheets under generally accepted accounting principles but which does not correspond to any contractual repayment obligation.

We believe that our cash, cash equivalents and marketable securities will be sufficient to fund our operations and capital expenditure requirements as currently planned for at least the next 12 months. This estimate does not reflect any additional expenditures resulting from additional sponsored research or the in-licensing or acquisition of additional product candidates or technologies or associated development that we may pursue following any such transactions. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Our capital requirements will depend on several factors, including the scope of any additional collaborative research programs, the success of our pursuit, by acquisition, in-licensing or otherwise, and subsequent development of additional product candidates or technologies, and the success of our ongoing development programs. We believe that we may need additional funding in the event that we acquire or in-license one or more additional product candidates and undertake development. In addition, our expenses may exceed our expectations if we experience delays in enrollment or with the availability of drug supply for our clinical trials, if we experience any unforeseen issues in our ongoing clinical trials or if we further expand the scope or size of our clinical trials and programs. Our costs may also exceed our expectations for other reasons, for example, if we experience issues with manufacturing or process development, or if we are required by the FDA, the EMA, or regulatory authorities in other jurisdictions to perform clinical or nonclinical trials or other studies in addition to those we currently expect to conduct. As a result, we may need or may seek to obtain additional funding in connection with our continuing operations sooner than expected.

The future development of our product candidates is highly uncertain. We expect the clinical development for Zimura will continue for at least the next several years. At this time, we cannot reasonably estimate the remaining costs necessary to complete clinical development, to complete process development and manufacturing scale-up and validation activities or to potentially seek marketing approval with respect to our product candidates.

Our future capital requirements, therefore, will depend on many factors, including:

- the scope, costs and results of our ongoing Zimura clinical programs, as well as any additional clinical trials we undertake to obtain data sufficient to seek marketing approval for Zimura in any indication;

- the extent to which we in-license or acquire rights to, and undertake research or development of products, product candidates or technologies, including any product candidate or other technologies we may evaluate as part of our collaborative gene therapy research programs;

- the amount of any upfront, milestone payments and other financial obligations associated with the in-license or acquisition of other product candidates;

- the scope, progress, results and costs of preclinical development and/or clinical trials for any other product candidates that we may develop;

- the costs and timing of process development, manufacturing scale-up and validation activities and ongoing stability studies associated with Zimura or any other product candidates that we may develop;

- our ability to establish collaborations on favorable terms, if at all;

- the costs, timing and outcome of regulatory reviews of our product candidates;

- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending intellectual property-related claims;

- the timing, scope and cost of commercialization activities for any of our product candidates if we receive, or expect to receive, marketing approval for a product candidate; and

- subject to receipt of marketing approval, net revenue received from commercial sales of any of our product candidates, after milestone payments and royalty payments that we would be obligated to make.

We do not have any committed external source of funds. Our future commercial revenues, if any, will be derived from sales of any of our product candidates that we are able to successfully develop, which may not be available for at least several years, if at all. In addition, if approved, our product candidates may not achieve commercial success. If that is the case, we will need to obtain substantial additional financing to achieve our business objectives. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Until such time, if ever, as we can generate substantial product revenues, we may need or may seek to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements.

Adequate additional financing may not be available to us on acceptable terms, or at all. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts.

In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, our existing stockholders' ownership interests would be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect their rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, products or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Licensing and Commercialization Agreement with Novartis Pharma AG

In May 2014, we entered into a licensing and commercialization agreement with Novartis Pharma AG, which we refer to as the Novartis Agreement. Under the Novartis Agreement, we granted Novartis exclusive rights under specified patent rights, know-how and trademarks controlled by us to manufacture, from bulk API supplied by us, standalone Fovista products and products combining Fovista with an anti-VEGF agent to which Novartis has rights in a co-formulated product, for the treatment, prevention, cure or control of any human disease, disorder or condition of the eye, and to develop and commercialize those licensed products in all countries outside of the United States, which we refer to as the Novartis Territory.

In July 2017, we and Novartis entered into a letter agreement to streamline the process and timeline for evaluating data from the OPH1004 trial once it became available. The letter agreement provides Novartis with a fully paid-up, royalty-free license to use data from the Lucentis monotherapy arms of our Phase 2b OPH1001 trial and Phase 3 OPH1002 and OPH1003 trials in the Novartis Territory in connection with the development, manufacturing and commercialization of Novartis-controlled anti-VEGF products. The Lucentis study data license shall continue until the fifth anniversary of the letter agreement or the date the Novartis Agreement expires or terminates, whichever is later. On October 23, 2017, following the failure of the Phase 3 Fovista program and pursuant to the terms of the Letter Agreement, Novartis elected to terminate the Novartis Agreement with immediate effect.

Novartis paid us a $200.0 million upfront fee upon execution of the Novartis Agreement. Novartis also paid us $50.0 million upon the achievement of each of two patient enrollment-based milestones, and $30.0 million upon the achievement of a third, and final, enrollment-based milestone, for an aggregate of $130.0 million.

Royalty Financing Agreement with Novo A/S

In May 2013, we entered into the Novo Agreement, pursuant to which we had the ability to obtain financing in three tranches in an amount of up to $125.0 million in return for the sale to Novo A/S of aggregate royalties of a mid-single-digit

percentage on worldwide sales of Fovista, with the royalty percentage determined by the amount of funding provided by Novo A/S. The three tranches of financing, in which Novo A/S purchased three low single-digit royalty interests and paid us $125.0 million in the aggregate, closed in May 2013, January 2014 and November 2014.

The royalty payment period begins on the commercial launch of Fovista and ends, on a country-by-country basis, on the latest to occur of the twelfth anniversary of the commercial launch of Fovista, the expiration of certain patent rights covering Fovista, and the expiration of regulatory exclusivity for Fovista, in each applicable country. Royalty payments will be payable quarterly in arrears during the royalty period. Our obligations under the Novo Agreement may also apply to certain other anti-PDGF, products we may develop.

We used a portion of the proceeds that we initially received under the Novo Agreement to repay in full an aggregate of $14.4 million of outstanding principal, interest and fees under our venture debt facility and used the remaining proceeds to support clinical development and regulatory activities for Fovista and for general corporate expenses.

The Novo Agreement requires the establishment by Novo A/S and us of a joint oversight committee in relation to the development of Fovista in the event that Novo A/S does not continue to have a representative on our board of directors. The Novo Agreement also contains customary representations and warranties, as well as certain covenants relating to the operation of our business, including covenants requiring us to use commercially reasonable efforts to complete the Phase 3 development of Fovista, to file, prosecute and maintain certain patent rights and, in our reasonable judgment, to pursue claims of infringement of our intellectual property rights. The Novo Agreement also places certain restrictions on our business, including restrictions on our ability to grant security interests in our intellectual property to third parties, to sell, transfer or out-license intellectual property, or to grant others rights to receive royalties on sales of Fovista and certain other products. We reimbursed Novo A/S for specified legal and other expenses and are required to provide Novo A/S with certain continuing information rights. We have agreed to indemnify Novo A/S and its representatives with respect to certain matters, including with respect to any third-party infringement or product liability claims relating to our products. Our obligations under the Novo agreement are secured by a lien on certain of our intellectual property and other rights related to Fovista and other anti-PDGF products we may develop.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2017:

	Payments Due by Period				
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
	(in thousands)				
Operating Leases (1)	$ 951	$ 895	$ 56	$ —	$ —
Severance and Other Employee Benefits (2)	2,529	2,529	—	—	—
Total (3)	$ 3,480	$ 3,424	$ 56	$ —	$ —

(1) The table above includes our continuing rent obligations through February 2020. On November 1, 2017, we and One Penn Plaza LLC entered into an amendment to the lease for office space at One Penn Plaza in New York, New York extending the term of our lease, which was scheduled to expire in January 2018, through the end of December 2018.

(2) Severance and Other Employee Benefits represents our commitments under the Board of Directors' approved plan to implement a reduction in personnel that involved approximately 80% of our workforce based on the number of employees at the time the plan was approved. The reduction in personnel was substantially completed during 2017 with a limited number of departing employees scheduled to receive severance payments during 2018.

(3) This table does not include (a) any milestone payments which may become payable to third parties under license agreements as the timing and likelihood of such payments are not known with certainty, (b) any royalty payments to third parties as the amounts, timing and likelihood of such payments are not known, (c) anticipated expenditures under supply agreements for periods for which we are not yet bound under binding purchase orders, (d) contracts that are entered into in the ordinary course of business that are not material in the aggregate in any period presented above and (e) our royalty purchase liability of $125.0 million as of December 31, 2017, due to the fact that royalty payment obligations are not expected given our lack of plans for the future development of Fovista or any other anti-PDGF product that would fall under our royalty obligation.

In addition to the amounts set forth in the table above, we may be required, under various agreements, to pay

royalties and make milestone payments. These agreements include the following:

- Under a license agreement with Archemix, for each anti-C5 aptamer product that we may develop under the agreement, including Zimura, we are obligated to make additional payments to Archemix of up to an aggregate of $57.5 million if we achieve specified development, clinical and regulatory milestones, with $30.5 million of such payments relating a first indication, $24.5 million of such payments relating to second and third indications and $2.5 million of such payments relating to sustained delivery applications. Under the C5 agreement, we are also obligated to make additional payments to Archemix of up to an aggregate of $22.5 million if we achieve specified commercial milestones based on net product sales of all anti-C5 products licensed under the agreement. We are also obligated to pay Archemix a double-digit percentage of specified non-royalty payments we may receive from any sublicensee of our rights under the C5 agreement. We are not obligated to pay Archemix a running royalty based on net product sales in connection with the C5 agreement.

We also have letter agreements with certain employees that require the funding of a specific level of payments, if certain events, such as a termination of employment in connection with a change in control or termination of employment by the employee for good reason or by us without cause, occur. For a description of these obligations, see our definitive proxy statement on Schedule 14A for our 2017 annual meeting of stockholders, as filed with the SEC on April 24, 2017.

In addition, in the course of normal business operations, we have agreements with contract service providers to assist in the performance of our research and development and manufacturing activities. Expenditures to CROs and CMOs represent significant costs in clinical development. Subject to required notice periods and our obligations under binding purchase orders, we can elect to discontinue the work under these agreements at any time. We could also enter into additional collaborative research, contract research, manufacturing, and supplier agreements in the future, which may require upfront payments and even long-term commitments of cash.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under Securities and Exchange Commission rules.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents and marketable securities of $167.0 million as of December 31, 2017, consisting of cash and investments in money market funds. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because a significant portion of our investments are in short-term securities. Our available for sale securities are subject to interest rate risk and will fall in value if market interest rates increase. Due to the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

We contract with CROs and CMOs globally. We may be subject to fluctuations in foreign currency rates in connection with certain of these agreements. Transactions denominated in currencies other than the U.S. dollar are recorded based on exchange rates at the time such transactions arise. As of December 31, 2017, substantially all of our total liabilities were denominated in the U.S. dollar.

Item 8. Financial Statements and Supplementary Data

Our financial statements, together with the report of our independent registered public accounting firm, appear on pages F-1 through F-25 of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2017. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Based on the evaluation of our disclosure controls and procedures as of December 31, 2017, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended (the Exchange Act). Our internal control over financial reporting is a process designed by, or under the supervision of our Chief Executive Officer and our Chief Financial Officer, and effected by the Company's board of directors, management and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2017. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in the original *Internal Control—Integrated Framework* updated in 2013. Based on that assessment, our management concluded that, as of December 31, 2017, our internal control over financial reporting was effective.

The effectiveness of the Company's internal control over financial reporting as of December 31, 2017, has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report which appears herein.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Ophthotech Corporation

Opinion on Internal Control over Financial Reporting

We have audited Ophthotech Corporation’s internal control over financial reporting as of December 31, 2017, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), (the COSO criteria). In our opinion, Ophthotech Corporation (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on the COSO criteria**.**

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the balance sheets of the Company as of December 31, 2017 and 2016, and the statements of operations, comprehensive income (loss), stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2017 and the related notes and our report dated March 5, 2018 expressed an unqualified opinion thereon.

Basis for Opinion

The Company’s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company’s internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company’s internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company’s internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company’s assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Iselin, New Jersey
March 5, 2018

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Directors and Executive Officers

The information required by this item will be set forth in our Proxy Statement for the 2018 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

Compliance with Section 16(a) of the Exchange Act

The information required by this item will be set forth in our Proxy Statement for the 2018 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

Code of Ethics

We have adopted a code of business conduct and ethics that applies to our directors and officers (including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions) as well as our other employees. A copy of our code of business conduct and ethics is available on our website. We intend to post on our website all disclosures that are required by applicable law, the rules of the Securities and Exchange Commission or the Nasdaq Global Market concerning any amendment to, or waiver of, our code of business conduct and ethics.

Director Nominees

The information required by this item will be set forth in our Proxy Statement for the 2018 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

Audit Committee

We have separately designated a standing Audit Committee established in accordance with Section 3(a)(58)(A) of the Exchange Act. Additional information regarding the Audit Committee that is required by this item will be set forth in our Proxy Statement for the 2018 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

Audit Committee Financial Expert

Our board of directors has determined that Jane Henderson is an "audit committee financial expert" as defined by Item 407(d)(5) of Regulation S-K of the Exchange Act and Ms. Henderson and the other members of our Audit Committee are "independent" under the rules of the Nasdaq Global Market.

Item 11. Executive Compensation

The information required by this item will be set forth in our Proxy Statement for the 2018 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item will be set forth in our Proxy Statement for the 2018 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item will be set forth in our Proxy Statement for the 2018 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

Item 14. Principal Accountant Fees and Services

The information required by this item will be set forth in our Proxy Statement for the 2018 Annual Meeting of Shareholders and is incorporated in this Annual Report on Form 10-K by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(1) Financial Statements

The following financial statements are filed as part of this Annual Report on Form 10-K:

(2) Financial Statement Schedules

No financial statement schedules have been filed as part of this Annual Report on Form 10-K because they are not applicable, not required or because the information is otherwise included in our financial statements or notes thereto.

(3) Exhibits

Exhibit Number		Description of Exhibit
3.1		Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.3 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-190643))
3.2		Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.4 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-190643))
4.1		Specimen Stock Certificate evidencing the shares of common stock (incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-190643))
10.1	+	Amended and Restated 2007 Stock Incentive Plan, as amended (incorporated by reference to Exhibit 10.1 of the Registrant's Registration Statement on Form S-1 (File No. 333-190643))
10.2	+	Form of Incentive Stock Option Agreement under Amended and Restated 2007 Stock Incentive Plan (incorporated by reference to Exhibit 10.2 of the Registrant's Registration Statement on Form S-1 (File No. 333-190643))
10.3	+	Form of Nonstatutory Stock Option Agreement under Amended and Restated 2007 Stock Incentive Plan (incorporated by reference to Exhibit 10.3 of the Registrant's Registration Statement on Form S-1 (File No. 333-190643))
10.4	+	2013 Stock Incentive Plan (incorporated by reference to Exhibit 10.4 of the Registrant's Annual Report on Form 10-K filed on March 2, 2015)
10.5	+	Amendment No. 1 to Stock Incentive Plan, adopted June 4, 2015 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q filed on August 10, 2015)
10.6	+	Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan (incorporated by reference to Exhibit 10.5 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-190643))
10.7	+	Form of Nonqualified Stock Option Agreement under 2013 Stock Incentive Plan (incorporated by reference to Exhibit 10.6 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-190643))
10.8	+	Form of Restricted Stock Unit Agreement under 2013 Stock Incentive Plan (incorporated by reference to Exhibit 10.7 of the Registrant's Annual Report on Form 10-K filed on March 2, 2015)
10.9	+	2016 Employee Stock Purchase Plan (incorporated by reference to Exhibit 99.1 of the Registrant's Registration Statement on Form S-8 (File No. 333-211916))

10.10		Lease Agreement, dated as of September 30, 2007, between the Registrant and One Penn Plaza LLC, as the same has been supplemented by agreement dated March 12, 2013 and amended by the Amendment of Lease, dated as of August 30, 2013, Second Amendment to Lease, entered into on January 7, 2014, Third Amendment of Lease, dated as of April 18, 2014, and the Fourth Amendment of Lease, dated as of December 22, 2014 (incorporated by reference to Exhibit 10.8 of the Registrant's Annual Report on Form 10-K filed on March 2, 2015)
10.11		Fifth Amendment of Lease, dated as of October 1, 2017, between the Registrant and One Penn Plaza LLC
10.12	†	Amended and Restated Exclusive License Agreement, dated as of September 12, 2011, by and between the Registrant and Archemix Corp., as amended by Amendment No. 1 thereto dated December 20, 2011 and supplemented by a letter agreement, dated as of April 30, 2012 (incorporated by reference to Exhibit 10.11 of the Registrant's Registration Statement on Form S-1 (File No. 333-190643))
10.13	†	Clinical and Commercial Services Agreement Between the Registrant and Ajinimoto Althea, Inc. dated October 31, 2016 (incorporated by reference to Exhibit 10.38 of the Registrant's Annual Report on Form 10-K filed on February 28, 2017)
10.14	+	Offer of Employment between the Registrant and David Guyer (incorporated by reference to Exhibit 10.14 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-190643))
10.15	+	Letter Agreement between the Registrant and David R. Guyer dated February 26, 2015, amending the Offer of Employment between the Registrant and David R. Guyer dated April 26, 2013 (incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q filed on May 11, 2015)
10.16	+	Letter Agreement between the Registrant and David R. Guyer, dated April 24, 2017 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q filed on August 2, 2017)
10.17	+	Letter Agreement between the Registrant and Glenn P. Sblendorio, dated January 4, 2016 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q filed on May 9, 2016)
10.18	+	Letter Agreement between the Registrant and Glenn P. Sblendorio, dated January 4, 2016 (incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q filed on May 9, 2016)
10.19	+	Letter Agreement between the Registrant and Glenn P. Sblendorio, dated April 24, 2017 (incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q filed on August 2, 2017)
10.20	+	Offer of Employment between the Registrant and Barbara A. Wood, dated October 21, 2013, revised October 22, 2013 (incorporated by reference to Exhibit 10.34 of the Registrant's Annual Report on Form 10-K filed on February 26, 2016)
10.21	+	Letter Agreement between the Registrant and Barbara A. Wood, dated February 20, 2015 (incorporated by reference to Exhibit 10.6 of the Registrant's Quarterly Report on Form 10-Q filed on May 11, 2015)
10.22	+	Separation and Release Agreement between the Registrant and Barbara A. Wood, dated January 5, 2018
10.23	+	Letter Agreement between the Registrant and David F. Carroll, dated April 25, 2017 (incorporated by reference to Exhibit 10.3 of the Registrant's Quarterly Report on Form 10-Q filed on August 2, 2017)
10.24	+	Promotion Letter between the Registrant and Keith Westby, dated January 30, 2017 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q filed on May 3, 2017)
10.25	+	Letter Agreement between the Registrant and Keith Westby, dated February 2, 2017 (incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q filed on May 3, 2017)
10.26	+	Form of Indemnification Agreement between the Registrant and each Director and Executive Officer (incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q filed on August 5, 2016)
23.1		Consent of Ernst & Young LLP
31.1		Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended
31.2		Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended
32.1		Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2		Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS		XBRL Instance Document
101.SCH		XBRL Taxonomy Extension Schema Document
101.CAL		XBRL Taxonomy Calculation Linkbase Document
101.DEF		XBRL Taxonomy Extension Definition Linkbase Document
101.LAB		XBRL Taxonomy Label Linkbase Document
101.PRE		XBRL Taxonomy Presentation Linkbase Document

† Confidential treatment has been granted as to certain portions, which portions have been omitted and separately filed with the Securities and Exchange Commission.

+ Management contract or compensatory plan or arrangement filed in response to Item 15(a)(3) of the Instructions to the Annual Report on Form 10-K.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: March 5, 2018

OPHTHOTECH CORPORATION

By: /s/ GLENN P. SBLENDORIO

Glenn P. Sblendorio
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1934, this report has been signed by the following persons on behalf of the registrant in the capacities and on the dates indicated.

Signature	Title	Date
/s/ GLENN P. SBLENDORIO Glenn P. Sblendorio	President, Chief Executive Officer and Director (principal executive officer)	March 5, 2018
/s/ DAVID F. CARROLL David F. Carroll	Senior Vice President and Chief Financial Officer (principal financial and accounting officer)	March 5, 2018
/s/ AXEL BOLTE Axel Bolte	Director	March 5, 2018
/s/ THOMAS DYRBERG Thomas Dyrberg, M.D., D.M.Sc.	Director	March 5, 2018
/s/ DAVID R. GUYER David R. Guyer, M.D.	Executive Chairman of the Board of Directors	March 5, 2018
/s/ JANE P. HENDERSON Jane P. Henderson	Director	March 5, 2018
/s/ DAVID E. REDLICK David E. Redlick	Director	March 5, 2018
/s/ MICHAEL ROSS Michael Ross, Ph.D.	Director	March 5, 2018

OPHTHOTECH CORPORATION

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Ophthotech Corporation

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Ophthotech Corporation (the Company) as of December 31, 2017 and 2016, the related statements of operations, comprehensive income (loss), stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2017, and the related notes (collectively referred to as the “financial statements”). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2017, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated March 5, 2018 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company’s financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company’s auditor since 2008.

Iselin, New Jersey

March 5, 2018

Ophthotech Corporation

Balance Sheets

(in thousands, except share and per share data)

	December 31, 2017	December 31, 2016
Assets		
Current assets		
Cash and cash equivalents	$ 166,972	$ 133,930
Available for sale securities	—	155,348
Due from Novartis Pharma AG	—	3,531
Prepaid expenses and other current assets	3,146	3,078
Income tax receivable	1,387	—
Total current assets	171,505	295,887
Property and equipment, net	518	3,281
Deferred tax assets	3,529	—
Other assets	24	462
Total assets	$ 175,576	$ 299,630
Liabilities and Stockholders' Equity (Deficit)		
Current liabilities		
Accrued research and development expenses	$ 4,984	$ 47,240
Accounts payable and accrued expenses	7,551	12,032
Deferred revenue	—	6,646
Total current liabilities	12,535	65,918
Deferred revenue, long-term	—	203,330
Royalty purchase liability	125,000	125,000
Total liabilities	137,535	394,248
Stockholders' equity (deficit)		
Preferred stock—$0.001 par value, 5,000,000 shares authorized, no shares issued or outstanding	$ —	$ —
Common stock—$0.001 par value, 200,000,000 shares authorized, 36,110,298 and 35,733,276 shares issued and outstanding at December 31, 2017 and December 31, 2016, respectively	36	36
Additional paid-in capital	522,759	504,517
Accumulated deficit	(484,754)	(598,959)
Accumulated other comprehensive loss	—	(212)
Total stockholders' equity (deficit)	38,041	(94,618)
Total liabilities and stockholders' equity (deficit)	$ 175,576	$ 299,630

The accompanying notes are an integral part of these financial statements.

Ophthotech Corporation

Statements of Operations

(in thousands, except per share data)

	Years ended December 31,		
	2017	**2016**	**2015**
Collaboration revenue	$ 209,977	$ 50,909	$ 51,505
Operating expenses:			
Research and development	66,289	196,295	131,012
General and administrative	35,683	50,178	44,021
Total operating expenses	101,972	246,473	175,033
Income (loss) from operations	108,005	(195,564)	(123,528)
Interest income	1,522	1,704	971
Other income (expense)	(34)	34	53
Income (loss) before income tax benefit	109,493	(193,826)	(122,504)
Income tax benefit	(4,712)	(406)	(16,787)
Net income (loss)	$ 114,205	$ (193,420)	$ (105,717)
Net income (loss) per common share:			
Basic	$ 3.18	$ (5.45)	$ (3.06)
Dilutive	3.17	(5.45)	(3.06)
Weighted average common shares outstanding:			
Basic	35,919	35,486	34,580
Dilutive	36,007	35,486	34,580

The accompanying notes are an integral part of these financial statements.

Ophthotech Corporation

Statements of Comprehensive Income (Loss)

(in thousands)

	Years ended December 31,		
	2017	**2016**	**2015**
Net loss	$ 114,205	$ (193,420)	$ (105,717)
Other comprehensive income (loss):			
Unrealized gain (loss) on available for sale securities, net of tax	212	261	(408)
Other comprehensive income (loss)	212	261	(408)
Comprehensive income (loss)	$ 114,417	$ (193,159)	$ (106,125)

The accompanying notes are an integral part of these financial statements.

Ophthotech Corporation

Statements of Stockholders' Equity (Deficit)

(in thousands)

	Junior Series A Preferred Stock		Common Stock		Additional paid-in capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total
	Shares	Amount	Shares	Amount				
Balance at December 31, 2014	—	$ —	33,995	$ 34	$ 428,390	$ (299,822)	$ (65)	$ 128,537
Issuance of common stock under employee stock compensation plans and warrants	—	—	1,202	1	11,472	—	—	11,473
Share-based compensation	—	—	—	—	24,760	—	—	24,760
Excess tax benefit from share-based compensation	—	—	—	—	1,302	—	—	1,302
Net loss	—	—	—	—	—	(105,717)	—	(105,717)
Unrealized loss on available for sale securities, net of tax	—	—	—	—	—	—	(408)	(408)
Balance at December 31, 2015	—	$ —	35,197	$ 35	$ 465,924	$ (405,539)	$ (473)	$ 59,947
Issuance of common stock under employee stock compensation plans and warrants	—	—	536	1	6,933	—	—	6,934
Share-based compensation	—	—	—	—	31,660	—	—	31,660
Net loss					—	(193,420)	—	(193,420)
Unrealized gain on available for sale securities, net of tax	—	—	—	—	—	—	261	261
Balance at December 31, 2016	—	$ —	35,733	$ 36	$ 504,517	$ (598,959)	$ (212)	$ (94,618)
Issuance of common stock under employee stock compensation plans	—	—	377	—	71	—	—	71
Share-based compensation	—	—	—	—	18,171	—	—	18,171
Net loss	—	—	—	—	—	114,205	—	114,205
Unrealized gain on available for sale securities, net of tax	—	—	—	—	—	—	212	212
Balance at December 31, 2017	—	$ —	36,110	$ 36	$ 522,759	$ (484,754)	$ —	$ 38,041

The accompanying notes are an integral part of these financial statements.

Ophthotech Corporation

Statements of Cash Flows

(in thousands)

	Years ended December 31,		
	2017	**2016**	**2015**
Operating Activities			
Net income (loss)	$ 114,205	$ (193,420)	$ (105,717)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities			
Depreciation	2,763	757	698
Amortization of premium and discounts on investment securities	140	595	2,846
Gain on sale of marketable securities	—	—	(57)
Deferred income taxes	(3,366)	22,954	(17,341)
Share-based compensation	18,171	31,660	24,760
Excess tax benefits from share-based compensation	—	—	(1,302)
Changes in operating assets and liabilities:			
Income tax receivable	(1,387)	3,421	48
Due from Novartis Pharma AG	3,531	858	(3,429)
Prepaid expense and other current assets	(68)	(995)	3,260
Accrued interest receivable	466	203	155
Other assets	438	27	(107)
Accrued research and development expenses	(42,256)	28,420	10,902
Accounts payable and accrued expenses	(4,481)	14	3,311
Deferred revenue	(209,977)	(3,090)	3,442
Net cash used in operating activities	(121,821)	(108,596)	(78,531)
Investing Activities			
Purchase of marketable securities	(12,014)	(72,197)	(411,565)
Sale of marketable securities	—	—	395,977
Maturities of marketable securities	166,806	86,500	266,000
Purchase of property and equipment	—	(572)	(2,615)
Proceeds from sale of assets	—	—	6
Net cash provided by investing activities	154,792	13,731	247,803
Financing Activities			
Proceeds from stock option/warrant exercises	71	6,934	11,473
Excess tax benefits from share-based compensation	—	—	1,302
Net cash provided by financing activities	71	6,934	12,775
Net change in cash and cash equivalents	33,042	(87,931)	182,047
Cash and cash equivalents			
Beginning of period	133,930	221,861	39,814
End of period	$ 166,972	$ 133,930	$ 221,861
Supplemental disclosure of cash paid			
Income taxes paid (received), net	$ (245)	$ (26,998)	$ 399
Supplemental disclosures of non-cash information related to investing activities			
Change in unrealized gain (loss) on available for sale securities, net of tax	$ 212	$ 261	$ (408)

The accompanying notes are an integral part of these financial statements.

Ophthotech Corporation

NOTES TO FINANCIAL STATEMENTS

(in thousands, except per share data)

1. Business

Description of Business and Organization

Ophthotech Corporation (the “Company” or “Ophthotech”) was incorporated on January 5, 2007, in Delaware. The Company is a science-driven biopharmaceutical company specializing in the development of novel therapies to treat ophthalmic diseases, with a focus on age-related and orphan retinal diseases. The Company's multi-track strategy is to leverage its clinical experience and retina expertise to develop therapies for large market, age-related retinal diseases, where unmet medical needs remain for these patients, and for orphan eye diseases with a focus on underserved patients, and to utilize a disciplined business development approach to obtain additional products, product candidates and technologies in these disease areas. The Company is developing Zimura® (avacincaptad pegol), its complement C5 inhibitor, for dry and wet forms of age-related macular degeneration, or AMD, which is a disorder of the central portion of the retina, known as the macula, that may result in loss of central vision, and autosomal recessive Stargardt disease, or STDG1, which is an orphan inherited retinal disease that also may result in loss of central and peripheral vision. The Company is actively engaged in extensive business development efforts to identify, evaluate and potentially obtain rights to and develop additional therapeutic and gene therapy product candidates that would complement its strategic goals and leverage its competitive advantages. The Company believes that its strategy will provide multiple potential opportunities to bring ophthalmic therapies to market.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented.

Segment and geographic information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating and reporting segment.

Use of Estimates

The preparation of financial statements and related disclosures in conformity with GAAP requires management to make estimates and judgments that affect the amounts reported in the financial statements and accompanying notes. The Company bases its estimates and judgments on historical experience and on various other assumptions that it believes are reasonable under the circumstances. The amounts of assets and liabilities reported in the Company's Balance Sheets and the amount of expenses reported for each of the periods presented are affected by estimates and assumptions, which are used for, but not limited to, accounting for research and development costs, revenue recognition, accounting for share-based compensation and accounting for income taxes. Actual results could differ from those estimates.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of 90 days or less when purchased to be cash equivalents. The carrying amounts reported in the Balance Sheets for cash and cash equivalents are valued at cost, which approximates their fair value.

As of December 31, 2017, the Company had cash and cash equivalents of approximately $167.0 million. The Company believes that its existing cash and cash equivalents as of December 31, 2017 will be sufficient to fund its operations and capital expenditure requirements as currently planned for at least the next 12 months.

Available for Sale Securities

The Company considers securities with original maturities of greater than 90 days when purchased to be available for sale securities. Available for sale securities with original maturities of greater than one year are recorded as non-current assets. Available for sale securities are recorded at fair value and unrealized gains and losses are recorded within accumulated other

comprehensive income (loss). The estimated fair value of the available for sale securities is determined based on quoted market prices or rates for similar instruments. In addition, the cost of debt securities in this category is adjusted for amortization of premium and accretion of discount to maturity. The Company evaluates securities with unrealized losses to determine whether such losses, if any, are other than temporary.

Revenue Recognition

Collaboration Revenue

In May 2014, the Company received an upfront payment of $200.0 million in connection with its licensing and commercialization agreement (the "Novartis Agreement") with Novartis Pharma AG ("Novartis"). Prior to the third quarter of 2017, this payment had not been recorded as revenue due to the existence of a contingency with respect to the Company's right to terminate the agreement in certain circumstances and the associated termination fee equivalent to the entire $200.0 million upfront payment, which the Company would have been required to pay if it had elected to exercise this termination option. The Company and Novartis entered into a letter agreement in July 2017 (the "Letter Agreement") that waived the Company's termination right, thereby resolving the contingency and allowing the Company to immediately recognize as revenue the portion of the upfront payment allocated using the relative selling price method to deliverables completed during prior periods. See "Note 5-Licensing and Commercialization Agreement with Novartis Pharma AG" below for a further description of the Letter Agreement. During the third quarter of 2017, the Company completed the remaining deliverables under the Novartis Agreement and the Letter Agreement and recognized as revenue the balance of all of the payments previously received from Novartis related to licensing, research and development, manufacturing and joint operating committee activities that had been previously deferred using the relative selling price method. In total, during the third quarter of 2017, the Company recognized $206.7 million in previously deferred collaboration revenue in connection with the Novartis Agreement. The recognition of this revenue during the period did not impact the Company's cash balance. On October 23, 2017, following the failure of the Phase 3 Fovista program and pursuant to the terms of the Letter Agreement, Novartis elected to terminate the Novartis Agreement with immediate effect. Below is a summary of the components of the Company's collaboration revenue for the years ended December 2017, 2016 and 2015:

	Years ended December 31,		
	2017	2016	2015
License revenue	$ 152,912	$ 22,937	$ 38,083
Research and development activity revenue	56,180	9,741	8,378
API transfer revenue	754	18,212	5,020
Joint operating committee revenue	131	19	24
Total collaboration revenue	$ 209,977	$ 50,909	$ 51,505

Concentration of Credit Risk

The Company's financial instruments that are exposed to concentration of credit risk consist primarily of cash and cash equivalents and available for sale securities. The Company maintains its cash in bank accounts, which generally exceed federally insured limits. The Company maintains its cash equivalents in investments in money market funds and, at times, in U.S. Treasury securities and investment-grade corporate debt securities with original maturities of 90 days or less.

The Company's available for sale securities are also invested in U.S. Treasury securities and investment-grade corporate debt securities. The Company believes it is not exposed to significant credit risk on its cash, cash equivalents and available for sale securities.

Concentration of Suppliers

The Company currently relies exclusively upon a single third-party manufacturer to provide supplies of the active pharmaceutical ingredient, or API, for Zimura on a purchase order basis. The Company also engages a single third-party manufacturer to provide fill/finish services for clinical supplies of Zimura. In addition, the Company currently relies upon a single third-party supplier to supply it with the proprietary polyethylene glycol, or PEG, reagent used to manufacture Zimura on a purchase order basis. Furthermore, the Company and its contract manufacturers currently rely upon sole-source suppliers of certain raw materials and other specialized components of production used in the manufacture and fill/finish of Zimura. If the Company's third-party manufacturers or fill/finish service providers should become unavailable to the Company for any reason, including as a result of capacity constraints, financial difficulties or insolvency, the Company believes that there are a limited number of potential replacement manufacturers, and the Company likely would incur added costs and delays in identifying or qualifying such replacements.

Foreign Currency Translation

The Company considers the U.S. dollar to be its functional currency. Expenses denominated in foreign currencies are translated at the exchange rate on the date the expense is incurred. The effect of exchange rate fluctuations on translating foreign currency assets and liabilities into U.S. dollars is included in the Statements of Operations. Foreign exchange transaction gains and losses are included in the results of operations and are not material in the Company's financial statements.

Financial Instruments

Cash equivalents and available for sale securities are reflected in the accompanying financial statements at fair value. The carrying amount of accounts payable and accrued expenses, including accrued research and development expenses, approximates fair value due to the short-term nature of those instruments.

Property and Equipment

Property and equipment, which consists mainly of manufacturing and clinical equipment, furniture and fixtures, computers, software, and other office equipment, and leasehold improvements, are carried at cost less accumulated depreciation. Depreciation is computed over the estimated useful lives of the respective assets, generally three to ten years, using the straight-line method. Amortization of leasehold improvements is recorded over the shorter of the lease term or estimated useful life of the related asset.

Research and Development

Research and development expenses primarily consist of costs associated with the manufacturing, development and clinical testing of Zimura and, historically, Fovista, as well as costs associated with the preclinical development of other product candidates and formulations. Research and development expenses consist of:

- external research and development expenses incurred under arrangements with third parties, such as contract research organizations ("CROs") and other vendors and contract manufacturing organizations ("CMOs") for the production of drug substance and drug product; and
- employee-related expenses, including salaries, benefits and share-based compensation expense.

Research and development expenses also include costs of acquired product licenses and related technology rights where there is no alternative future use, costs of prototypes used in research and development, consultant fees and amounts paid to collaborative partners. The Company expects that research and development expenses in the future will also include the costs of the Company's collaborative gene therapy research programs.

All research and development expenses are charged to operations as incurred in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic, or ASC, 730, *Research and Development*. The Company accounts for non-refundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received, rather than when the payment is made.

Income Taxes

The Company utilizes the liability method of accounting for deferred income taxes, as set forth in ASC 740, *Income Taxes*. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities.

Share-Based Compensation

The Company follows the provisions of ASC 718, *Compensation—Stock Compensation*, which requires the measurement and recognition of compensation expense for all share-based payment awards made to employees and non-employee directors, including employee stock options, restricted stock units (“RSUs”) and the option granted to employees to purchase shares under the 2016 Employee Stock Purchase Plan (the “ESPP”). Share-based compensation expense is based on the grant date fair value estimated in accordance with the provisions of ASC 718 and is generally recognized as an expense over the requisite service period, net of estimated forfeitures. For grants containing performance-based vesting provisions, expense is recognized over the estimated achievement period.

Stock Options

The Company estimates the fair value of stock options granted to employees and non-employee directors on the date of grant using the Black-Scholes option-pricing model. Due to the lack of trading history, the Company's computation of stock-price volatility is based on the volatility rates of comparable publicly held companies over a period equal to the expected term

of the options granted by the Company. The Company's computation of expected term is determined using the "simplified" method, which is the midpoint between the vesting date and the end of the contractual term. The Company believes that it does not have sufficient reliable exercise data in order to justify the use of a method other than the "simplified" method of estimating the expected exercise term of employee stock option grants. The Company utilizes a dividend yield of zero based on the fact that the Company has never paid cash dividends to stockholders and has no current intentions to pay cash dividends. The risk-free interest rate is based on the zero-coupon U.S. Treasury yield at the date of grant for a term equivalent to the expected term of the option.

For stock options granted as consideration for services rendered by consultants, the Company recognizes expense in accordance with the requirements of ASC 505-50, *Equity Based Payments to Non-Employees*. Consultant stock option grants are recorded as an expense over the vesting period of the underlying stock options. At the end of each financial reporting period prior to vesting, the value of these options, as calculated using the Black-Scholes option-pricing model, will be re-measured using the fair value of the Company's common stock and the non-cash expense recognized during the period will be adjusted accordingly. Since the fair value of options granted to consultants is subject to change in the future, the amount of the future expense will include fair value re-measurements until the stock options are fully vested.

The weighted-average assumptions used to estimate grant date fair value of stock options using the Black-Scholes option pricing model were as follows for the years ended December 31, 2017, 2016 and 2015:

	Years ended December 31,		
	2017	2016	2015
Expected common stock price volatility	81%	71%	72%
Risk-free interest rate	1.82% - 2.38%	1.14% - 2.37%	1.35% - 2.24%
Expected term of options (years)	6.1	6.1	6.2
Expected dividend yield	—	—	—

RSUs

The Company estimates the fair value of RSUs granted to employees using the closing market price of the Company's common stock on the date of grant.

ESPP

In April 2016, the board of directors adopted the ESPP pursuant to which the Company may sell up to an aggregate of 1,000,000 shares of common stock. The ESPP was approved by the Company’s stockholders in June 2016. The ESPP is considered compensatory and the fair value of the discount and look back provision are estimated using the Black-Scholes option-pricing model and recognized over the six month withholding period prior to purchase.

Share-based compensation expense includes expenses related to stock options and RSUs granted to employees, non-employee directors and consultants, as well as the option granted to employees to purchase shares under the ESPP, all of which have been reported in the Company’s Statements of Operations as follows:

	Years ended December 31,		
	2017	2016	2015
Research and development	$ 11,114	$ 21,380	$ 16,608
General and administrative	7,057	10,280	8,152
Total	$ 18,171	$ 31,660	$ 24,760

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2014-9, *Revenue from Contracts with Customers (Topic 606)* (“ASU 2014-9”). ASU 2014-9 outlines a new, single comprehensive model for entities to use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance, including industry-specific guidance. This new revenue recognition model provides a five-step analysis in determining when and how revenue is recognized. The new model will require revenue recognition to depict the transfer of promised goods or services to customers in an amount that reflects the consideration a company expects to receive in exchange for those goods or services. The FASB subsequently issued additional clarifying standards to address issues arising from implementation of the new revenue standard, including a one-year deferral of the effective date for the new

revenue standard. Public companies should now apply the guidance in ASU 2014-9 to annual reporting periods beginning after December 15, 2017 and interim periods within those annual periods. Earlier application is permitted only as of annual reporting periods beginning after December 15, 2016, including interim periods within that annual period. Companies may use either a full retrospective or a modified retrospective approach to adopt ASU 2014-9. Due to the recent development and termination of the Company's collaboration contracts with Novartis, the Company will not be impacted upon adoption of this standard.

In February 2016, the FASB issued ASU No. 2016-2, *Leases (Topic 842)*. Under the new guidance, lessees will be required to recognize the following for all leases (with the exception of short-term leases) at the commencement date: (1) a lease liability, which is a lessee's obligation to make lease payments arising from a lease, measured on a discounted basis; and (2) a right-of-use asset, which is an asset that represents the lessee's right to use, or control the use of, a specified asset for the lease term. Under the new guidance, lessor accounting is largely unchanged. Certain targeted improvements were made to align, where necessary, lessor accounting with the lessee accounting model and Topic 606, *Revenue from Contracts with Customers*. The new lease guidance simplified the accounting for sale and leaseback transactions primarily because lessees must recognize lease assets and lease liabilities. Lessees will no longer be provided with a source of off-balance sheet financing. Publicly-traded business entities should apply the amendments in ASU 2016-2 for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years (i.e., January 1, 2019, for a calendar year entity). Early application is permitted for all publicly-traded business entities and all nonpublicly-traded business entities upon issuance. Lessees (for capital and operating leases) and lessors (for sales-type, direct financing, and operating leases) must apply a modified retrospective transition approach for leases existing at, or entered into after, the beginning of the earliest comparative period presented in the financial statements. The modified retrospective approach would not require any transition accounting for leases that expired before the earliest comparative period presented. Lessees and lessors may not apply a full retrospective transition approach. The Company is currently assessing the impact that adopting this new accounting guidance will have on its financial statements and footnote disclosures.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments*, which clarifies the presentation of certain specific cash flow issues in the Statement of Cash Flows. For public companies, the amendments are effective for annual reporting periods beginning after December 15, 2017, and interim periods within those annual periods and early adoption is permitted. This new guidance is not expected to have a material impact on the Company's Consolidated Financial Statements.

In January 2017, the FASB issued ASU No. 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business*, in an effort to clarify the definition of a business with the objective of adding guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The amendments of this ASU are effective for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. Early adoption is permitted. This new guidance will be applicable for the Company's acquisitions on or after January 1, 2018.

3. Net Income (Loss) Per Common Share

Basic and diluted net income (loss) per common share is determined by dividing net income (loss) by the weighted average common shares outstanding during the period. For the periods where there is a net loss, stock options and RSUs have been excluded from the calculation of diluted net loss per common share because their effect would be anti-dilutive. Therefore, the weighted average common shares used to calculate both basic and diluted net loss per common share would be the same. The following table sets forth the computation of basic and diluted net income (loss) per common share for the periods indicated:

	Years ended December 31,		
	2017	2016	2015
Basic and diluted net income (loss) per common share calculation:			
Net loss	$ 114,205	$ (193,420)	$ (105,717)
Weighted average common shares outstanding - basic	35,919	35,486	34,580
Plus: net effect of dilutive stock options and unvested restricted stock units	88	—	—
Weighted average common shares outstanding - dilutive	36,007	35,486	34,580
Net income (loss) per common share - basic	$ 3.18	$ (5.45)	$ (3.06)
Net income (loss) per common share - diluted	$ 3.17	$ (5.45)	$ (3.06)

The following potentially dilutive securities have been excluded from the computations of diluted weighted average common shares outstanding for the periods presented, as they would be anti-dilutive:

	Years ended December 31,		
	2017	2016	2015
Stock options outstanding	5,179	3,359	3,009
Restricted stock units	182	721	288
Total	5,361	4,080	3,297

4. Cash, Cash Equivalents and Available for Sale Securities

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at the date of purchase to be cash equivalents. Cash and cash equivalents included cash of $9.5 million and $25.8 million at December 31, 2017 and 2016, respectively. Cash and cash equivalents at December 31, 2017 and December 31, 2016 also included $157.4 million and $108.1 million, respectively, of investments in money market funds, U.S. Treasury securities and certain short-term investment-grade corporate debt securities with original maturities of 90 days or less.

The Company considers securities with original maturities of greater than 90 days at the date of purchase to be available for sale securities. The Company held no available for sale securities at December 31, 2017. At December 31, 2016, the Company held available for sale securities with a fair value totaling $155.3 million. These available for sale securities consisted of U.S. Treasury securities and investment-grade corporate debt securities. During the year ended December 31, 2017, the Company's investments matured and were reinvested in money market funds.

Available for sale securities, including carrying value and estimated fair values, are summarized as follows:

	As of December 31, 2016			
	Cost	Unrealized Gains	Unrealized Losses	Fair Value
U.S. Treasury securities	$ 120,288	$ 6	$ (33)	$ 120,261
Corporate debt securities	35,114	—	(27)	35,087
Total	$ 155,402	$ 6	$ (60)	$ 155,348

The Company's available for sale securities are reported at fair value on the Company's Balance Sheets. Unrealized gains (losses) are reported within accumulated other comprehensive income (loss) in the statements of comprehensive income (loss). The cost of securities sold and any realized gains/losses from the sale of available for sale securities are based on the specific identification method. The changes in accumulated other comprehensive income (loss) associated with the unrealized gain (loss) on available for sale securities for the years ended December 31, 2017 and December 31, 2016 were as follows:

	Years ended December 31,	
	2017	2016
Beginning balance	$ (212)	$ (473)
Current period changes in fair value before reclassifications, net of tax	212	261
Amounts reclassified from accumulated other comprehensive income (loss), net of tax	—	—
Total other comprehensive income (loss)	212	261
Ending balance	$ —	$ (212)

5. Licensing and Commercialization Agreement with Novartis Pharma AG

In May 2014, the Company entered into the Novartis Agreement. Under the Novartis Agreement, the Company granted Novartis exclusive rights under specified patent rights, know-how and trademarks controlled by the Company to manufacture, from bulk API supplied by the Company, standalone Fovista products and products combining Fovista with an anti-VEGF agent to which Novartis has rights in a co-formulated product, for the treatment, prevention, cure or control of any human disease, disorder or condition of the eye, and to develop and commercialize those licensed products in all countries outside of the United States (the “Novartis Territory”). The Company agreed to use commercially reasonable efforts to complete its ongoing pivotal Phase 3 clinical program for Fovista and Novartis agreed to use commercially reasonable efforts to

develop a standalone Fovista product and a co-formulated product containing Fovista and an anti-VEGF agent to which Novartis has rights, as well as a pre-filled syringe presentation of such products and to use commercially reasonable efforts, subject to obtaining marketing approval, to commercialize licensed products in the Novartis Territory in accordance with agreed development and marketing plans.

In July 2017, the Company and Novartis entered into the Letter Agreement to streamline the process and timeline for evaluating data from the OPH1004 trial once it became available. On October 23, 2017, following the failure of the Phase 3 Fovista program and pursuant to the terms of the Letter Agreement, Novartis elected to terminate the Novartis Agreement with immediate effect.

In May 2014, Novartis paid the Company a $200.0 million upfront payment. In each of September 2014 and March 2015, the Company achieved a $50.0 million enrollment-based milestone, and in June 2016, the Company achieved a $30.0 million enrollment-based milestone, for an aggregate total of $130.0 million in enrollment-based milestones under the Novartis Agreement. The Company used the relative selling price method to allocate these payments to contract deliverables based on its performance obligations under the Novartis Agreement.

Activities under the Novartis Agreement were evaluated under ASC 605-25, *Revenue Recognition—Multiple Element Arrangements* (“ASC 605-25”) (as amended by ASU 2009-13, *Revenue Recognition* (“ASU 2009-13”)) to determine if they represented a multiple element revenue arrangement. The Novartis Agreement included the following deliverables: (1) an exclusive license to commercialize Fovista outside the United States (the “License Deliverable”); (2) the performance obligation to conduct research and development activities related to the Phase 3 Fovista clinical trials and certain Phase 2 trials for Fovista (the “R&D Activity Deliverable”); (3) the performance obligation to supply API to Novartis for development and manufacturing purposes (the “Manufacturing Deliverable”) and (4) the Company’s obligation to participate on the joint operating committee established under the terms of the Novartis Agreement and related subcommittees (the “Joint Operating Committee Deliverable”). The Company’s obligation to provide access to clinical and regulatory information as part of the License Deliverable included the obligation to provide access to all clinical data, regulatory filings, safety data and manufacturing data to Novartis which was necessary for the commercialization of Fovista in the Novartis Territory. The R&D Activity Deliverable included the right and responsibility for the Company to conduct the Phase 3 Fovista clinical program and other Phase 2 studies of Fovista which were necessary or desirable for regulatory approval or commercialization of Fovista. The Manufacturing Deliverable included the obligation for the Company to supply API to Novartis for clinical purposes, for which Novartis agreed to pay the Company’s manufacturing costs. The Joint Operating Committee Deliverable included the obligation to participate in the Joint Operating Committee and related subcommittees at least through the first anniversary of regulatory approval in the European Union. All of these deliverables were deemed to have stand-alone value and to meet the criteria to be accounted for as separate units of accounting under ASC 605-25. Factors considered in this determination included, among other things, the subject of the licenses and the research and development and commercial capabilities of Novartis. Accordingly, each unit was accounted for separately.

The Novartis Agreement included a termination right for the Company in the event that specified governmental actions prevented the parties from materially progressing the development or commercialization of licensed products. If the Company elected to exercise this termination option, it would have been required to pay a substantial termination fee equivalent to the entire upfront payment amount. The Company concluded that this termination provision constituted a contingent event that was unknown at the inception of the agreement. As such, the Company recorded the $200.0 million upfront payment in deferred revenue, long-term until such time that the contingency related to this termination provision was resolved. In July 2017, the contingency was resolved when the Company permanently waived this termination right as part of the Letter Agreement.

The Letter Agreement also provided Novartis with a shorter notice period in the event Novartis determined to terminate the Novartis Agreement in certain circumstances. In addition, the Letter Agreement provided Novartis with a fully paid-up, royalty free license to use data from the Lucentis monotherapy arms of the Company's Phase 2b OPH1001 trial and Phase 3 OPH1002 and OPH1003 trials in the Novartis Territory in connection with the development, manufacturing and commercialization of Novartis-controlled anti-VEGF products. The Lucentis study data license continues until the fifth anniversary of the Letter Agreement.

The Company evaluated the Letter Agreement under ASC 605-25 and determined that the Letter Agreement does not create any new deliverables. The Company is treating the Fovista license granted at the inception of the Novartis Agreement and the Lucentis study data license granted under the Letter Agreement as one collective technology license (the "Licenses") delivered at the inception of the Novartis Agreement. In addition, as the waiver of its right to terminate the Novartis Agreement as a result of specified governmental actions resolved the Company’s contingency with respect to such termination right and the associated termination fee, the Company allocated the entire previously deferred amount, $200.0 million, to the deliverables

that were determined based on the relative selling price at contract inception. Upon entry into the Letter Agreement in July 2017, the Company immediately recognized as revenue $189.8 million of the upfront payment allocated to contract deliverables completed during prior periods. Upon termination of the OPH1004 trial in August 2017, the Company recognized the remaining $16.9 million of collaboration revenue, attributable to the R&D Deliverable, previously deferred under the Novartis Agreement. In total, during the third quarter of 2017, the Company recognized $206.7 million in previously deferred collaboration revenue in connection with the Novartis Agreement. The recognition of this revenue during the period did not impact the Company's cash balance.

Below is a summary of the components of the Company's collaboration revenue for the years ended December 31, 2017, 2016, and 2015:

	Years ended December 31,		
	2017	2016	2015
License revenue	$ 152,912	$ 22,937	$ 38,083
Research and development activity revenue	56,180	9,741	8,378
API transfer revenue	754	18,212	5,020
Joint operating committee revenue	131	19	24
Total collaboration revenue	$ 209,977	$ 50,909	$ 51,505

6. Financing Agreement with Novo A/S

In May 2013, the Company entered into a Purchase and Sale Agreement with Novo A/S, which is referred to as the Novo Agreement, pursuant to which the Company had the ability to obtain financing in three tranches in an amount of up to $125.0 million in return for the sale to Novo A/S of aggregate royalties of worldwide sales of (a) Fovista, (b) Fovista-Related Products, and (c) Other Products (each as defined in the Novo Agreement), calculated as mid-single digit percentages of net sales.

The Novo Agreement provided for up to three separate purchases for a purchase price of $41.7 million each, at a first, second and third closing, for an aggregate purchase price of $125.0 million. In each purchase, Novo A/S would acquire rights to a low single digit percentage of net sales. In each of May 2013, January 2014 and November 2014, the Company received cash payments of $41.7 million, or $125.0 million in the aggregate, and Novo A/S received, in the aggregate, a right to receive royalties on net sales of Fovista at a mid-single digit percentage.

The royalty payment period covered by the Novo Agreement begins on commercial launch and ends, on a product-by-product and country-by-country basis, on the latest to occur of (i) the 12th anniversary of the commercial launch, (ii) the expiration of certain patent rights and (iii) the expiration of the regulatory exclusivity for each product in each country. The Company's obligations under the Novo agreement are secured by a lien on certain of the Company's intellectual property and other rights related to Fovista and other anti-PDGF products the Company may develop.

Under the terms of the Novo Agreement, the Company is not required to reimburse or otherwise compensate Novo A/S through any means other than the agreed royalty entitlement. In addition, the Company does not, under the terms of the Novo Agreement, have the right or obligation to prepay Novo A/S in connection with a change of control of the Company or otherwise.

The $125.0 million in aggregate proceeds from the three financing tranches under the Novo Agreement represents the full funding available under the Novo Agreement, and has been recorded as a liability on the Company's Balance Sheet as of December 31, 2017, in accordance with ASC 730, *Research and Development*. Because there is a significant related party relationship between the Company and Novo A/S, the Company is treating its obligation to make royalty payments under the Novo Agreement as an implicit obligation to repay the funds advanced by Novo A/S. As the Company makes royalty payments in accordance with the Novo Agreement, it will reduce the liability balance. At the time that such royalty payments become probable and estimable, and if such amounts exceed the liability balance, the Company will impute interest accordingly on a prospective basis based on such estimates.

The Novo Agreement requires the establishment of a Joint Oversight Committee in the event that Novo A/S does not continue to have a representative on the Company's board of directors. The Joint Oversight Committee would have responsibilities that include "discussion and review" of all matters related to Fovista research, development, regulatory approval and commercialization, but there is no provision either implicit or explicit that gives the Joint Oversight Committee or its members decision-making authority.

7. Property and Equipment

Property and equipment as of December 31, 2017 and 2016 were as follows:

	Useful Life (Years)	December 31, 2017	December 31, 2016
Manufacturing and clinical equipment	7 - 10	$ 412	$ 617
Computer, software and other office equipment	5	933	1,711
Furniture and fixtures	7	—	774
Leasehold improvements	3 - 5	—	1,835
		1,345	4,937
Accumulated depreciation		(827)	(1,656)
Property and equipment, net		$ 518	$ 3,281

For the years ended December 31, 2017, 2016 and 2015, depreciation expense was $2.8 million, $0.8 million and $0.7 million, respectively.

8. Income Taxes

On December 22, 2017, the U.S. Tax Cuts and Jobs Act (“TCJA”) was enacted reducing the corporate tax rate from 35% to 21% effective for tax years beginning on or after January 1, 2018. ASC 740, Income Taxes requires the effects of changes in tax laws to be recognized in the period in which the legislation is enacted. However, due to the complexity and significance of the Tax Act’s provisions, the SEC staff issued SAB 118, which allows companies to record the tax effects of the TCJA on a provisional basis based on a reasonable estimate, and then, if necessary, subsequently adjust such amounts during a limited measurement period as more information becomes available. The measurement period ends when a company has obtained, prepared, and analyzed the information necessary to finalize its accounting, but cannot extend beyond one year from enactment.

Under the TCJA, the Corporate Alternative Minimum Tax ("AMT") was repealed. The Company's previously recorded Alternative Minimum Tax (“AMT”) credits of approximately $3.5 million are now refundable over a four year period beginning in 2018 and the previously recorded valuation allowance for these AMT credits was reversed during the year ended December 31, 2017. As a result of the reduction in the corporate tax rate from 35% to 21% the value of the Company’s deferred tax assets, and related valuation allowance, were reduced by a provisional amount of approximately $54.6 million. The Company does not have any offshore earnings from which to record the mandatory transition tax. Given the significant complexity of the TCJA, anticipated guidance from the US Treasury about implementing the TCJA, and the potential for additional guidance from the SEC or the FASB related to the TCJA, the deferred taxes provisional amounts may be adjusted during the measurement period. These provisional amounts were based on the Company’s present interpretations of the TCJA and current available information, including assumptions and expectations about future events, such as its projected financial performance, and are subject to further refinement as additional information becomes available (including potential new or interpretative guidance issued by the FASB or the Internal Revenue Service and other tax agencies) and further analyses are completed.

The Company utilizes the liability method of accounting for deferred income taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities. A valuation allowance is established against deferred tax assets when, based on the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company's policy is to record interest and penalties on uncertain tax positions as income tax expense.

Deferred income taxes reflect the net effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. A reconciliation of the statutory U.S. federal rate to the Company's effective tax rate is as follows:

	Years ended December 31,		
	2017	2016	2015
Percent of pre-tax income:			
U.S. federal statutory income tax rate	35.0 %	35.0 %	35.0 %
State taxes, net of federal benefit	14.6 %	2.8 %	7.4 %
Permanent items	4.0 %	(1.4)%	(0.5)%
Remeasurement of deferred tax assets	49.9 %	— %	— %
Impact of state rate changes	(27.9)%	(11.0)%	0.9 %
Research and development credit	— %	1.9 %	— %
Alternative minimum tax credit	(1.3)%	1.1 %	— %
Change in valuation allowance	(78.6)%	(28.2)%	(29.1)%
Effective income tax rate	(4.3)%	0.2 %	13.7 %

The components of income tax (benefit) expense are as follows:

	Years ended December 31,		
	2017	2016	2015
Current:			
Federal	$ 173	$ (23,393)	$ 136
State	(1,356)	21	91
Deferred:			
Federal	(3,529)	22,966	(17,014)
State	—	—	—
Income tax benefit	$ (4,712)	$ (406)	$ (16,787)

Significant components of the Company's deferred tax assets (liabilities) for 2017 and 2016 consist of the following:

	As of December 31,	
	2017	2016
Deferred tax assets (liabilities)		
Deferred revenue	$ 40,961	$ 125,634
License and technology payments	8,222	10,532
Share-based compensation	17,599	16,494
Accrued expenses	608	530
Depreciation	81	(651)
Federal and state net operating loss carryforwards	76,309	75,177
Research and development credits	3,782	3,720
Other	3,534	2,155
Deferred income tax assets	151,096	233,591
Valuation allowance	(147,567)	(233,591)
Net deferred tax assets	$ 3,529	$ —

In assessing the realizability of deferred tax assets, the Company considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of taxable income during the periods in which the temporary differences representing net future deductible amounts become deductible.

The Company incurred tax losses in 2017 and 2016. The Company realized its net deferred tax assets recorded as of December 31, 2016 in 2016 as a result of the Company's carry back of its 2015 federal tax losses to 2014. The Company has carried forward its 2015 state tax losses due to various state restrictions on the use of carryback claims. The state NOLs are expected to begin to expire in 2027. Due to the Company's history of losses and lack of other positive evidence to support taxable income after the 2014 tax year, the Company has recorded a valuation allowance against those remaining deferred tax assets that are not expected to be realized. As of December 31, 2017, the Company has federal NOL carryforwards of approximately $270.0 million. These losses are due to expire in 2036 and 2037.

For the year ended December 31, 2017, the Company recorded an income tax benefit of $4.7 million which primarily related to a $3.5 million reduction in our valuation allowances for AMT credits to reflect the impact of the TCJA enactment and a settlement of a state franchise tax audit for $1.4 million partially offset by the reversal of previously recoded benefits related to the change in unrealized gains of the Company's investment portfolio. Although the Company generated $109.5 million of net income before income taxes for the year ended December 31, 2017 as a result of the recognition of deferred revenue under the Novartis Agreement, the Company expects a net loss for tax purposes for 2017 with minimal taxes due. For tax purposes, the Company treated payments received under the Novartis Agreement as revenue at the time the payments were received. The benefit from income taxes of $0.4 million recorded in 2016 was related to unanticipated refunds received and the reduction in the Company's valuation allowances to reflect the income tax associated with unrealized gains in the Company's investment portfolio.

In the second quarter of 2017, the IRS concluded an audit of the Company's U.S. federal income tax returns for the years 2013, 2014 and 2015, resulting in an immaterial amount of additional tax due. Federal net operating losses for 2016 and general business credits generated between 2007 and 2016 remain subject to audit.

Pursuant to ASC 740, *Income Taxes*, the Company routinely evaluates the likelihood of success if challenged on income tax positions claimed on its income tax returns. During the year ended December 31, 2017, the Company reduced certain deferred tax assets by $6.2 million and reduced the corresponding valuation allowance by an equivalent amount. Additionally, the Company amended certain state income tax returns to claim a refund for taxes previously paid. These claims may result in refunds to the Company of up to approximately $6.5 million. These items have not been recognized in the financial statements and if disallowed by the tax authorities, would not result in an adjustment to the Company's effective tax rate, its balance sheet or its cash flow statements for the current year.

The Company's position with respect to uncertain tax positions is set forth below:

Opening balance	$	4,128
Gross amount of increases in unrecognized tax benefits during the period - current year provisions		343
Gross amount of increases in unrecognized tax benefits during the period - prior year provisions		14,430
Gross amount of increases in unrecognized tax benefits during the period - other		—
Decreases due to settlement with tax authorities during the period		(2,020)
Reduction of unrecognized tax benefits due to expiration of the state of limitations during the period		—
Closing Balance	$	16,881

As the Company is currently being audited by the New York City Department of Finance and the New Jersey Division of Taxation, an estimate of unrecognized tax benefits that may be realized over the next twelve months is expected to be in the range of zero to approximately $6.9 million.

The Company will continue to evaluate its ability to realize its deferred tax assets on a periodic basis and will adjust such amounts in light of changing facts and circumstances including, but not limited to, future projections of taxable income, tax legislation, rulings by relevant tax authorities, the progress of ongoing tax audits and the regulatory approval of products currently under development. Any additional changes to the valuation allowance recorded on deferred tax assets in the future would impact the Company's income taxes.

9. Operating Leases

The Company leases office space located in New York, New York and Princeton, New Jersey under operating lease arrangements. The lease for the Company's New York office space expires at the end of 2018, whereas the lease for the Company's Princeton office space expires in March 2020. Future minimum rental commitments under non-cancelable operating leases in effect as of December 31, 2017, are as follows:

2018	$	895
2019		48
2020		8
Total	$	951

Rent expense is calculated on the straight-line basis and amounted to $3.6 million, $3.0 million and $2.1 million for the years ended December 31, 2017, 2016 and 2015, respectively. In January 2017, the Company terminated its office leases in New York, New York and Princeton, New Jersey and made aggregate termination payments of approximately $2.1 million.

10. Commitments and Contingencies

Under various agreements, the Company may be required to pay royalties and make milestone payments. These agreements include the following:

- Under a license agreement with Archemix Corp., or Archemix, for each anti-C5 aptamer product that the Company may develop under the agreement, including Zimura, the Company is obligated to make additional payments to Archemix of up to an aggregate of $57.5 million if the Company achieves specified development, clinical and regulatory milestones, with $30.5 million of such payments relating a first indication, $24.5 million of such payments relating to second and third indications and $2.5 million of such payments relating to sustained delivery applications. Under the C5 agreement, the Company is also obligated to make additional payments to Archemix of up to an aggregate of $22.5 million if the Company achieves specified commercial milestones based on net product sales of all anti-C5 products licensed under the agreement. The Company is also obligated to pay Archemix a double-digit percentage of specified non-royalty payments the Company may receive from any sublicensee of its rights under the C5 agreement. The Company is not obligated to pay Archemix a running royalty based on net product sales in connection with the C5 agreement.

The Company also has letter agreements with certain employees that require the funding of a specific level of payments, if certain events, such as a termination of employment in connection with a change in control or termination of employment by the employee for good reason or by the Company without cause, occur.

In addition, in the course of normal business operations, the Company has agreements with contract service providers to assist in the performance of the Company’s research and development and manufacturing activities. Expenditures to CROs and CMOs represent significant costs in clinical development. Subject to required notice periods and the Company’s obligations under binding purchase orders, the Company can elect to discontinue the work under these agreements at any time.

Legal Proceedings

On January 11, 2017, a putative class action lawsuit was filed against the Company and certain of its current and former executive officers in the United States District Court for the Southern District of New York, captioned Frank Micholle v. Ophthotech Corporation, et al., No. 1:17-cv-00210. The complaint purports to be brought on behalf of shareholders who purchased the Company's common stock between May 11, 2015 and December 12, 2016. The complaint generally alleges that the Company and certain of its officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the prospects of the Company's Phase 3 trials for Fovista in combination with anti-VEGF agents for the treatment of wet AMD. The complaint seeks equitable and/or injunctive relief, unspecified damages, attorneys’ fees, and other costs.

On March 9, 2017, a second putative class action lawsuit was filed against the Company and the same group of its current and former executive officers in the United States District Court for the Southern District of New York, captioned Wasson v. Ophthotech Corporation, et al., No. 1:17-cv-01758. The complaint purports to be brought on behalf of shareholders who purchased the Company’s common stock between May 11, 2015 and December 9, 2016. The allegations made in the

complaint are similar to those made in the Micholle complaint. Putative lead plaintiffs in the Micholle action have moved to consolidate the Micholle and Wasson actions.

On February 7, 2018, a shareholder derivative action was filed against the members of the Company's Board of Directors in the New York Supreme Court Commercial Division, captioned Cano v. Guyer, et al., No. 650601/2018. The complaint alleges that defendants breached their fiduciary duties to the Company by adopting a compensation plan that overcompensates the non-employee members of the Board relative to boards of companies of comparable market capitalization and size. The complaint also alleges that defendants were unjustly enriched as a result of the alleged conduct. The complaint purports to seek unspecified damages on behalf of the Company, as well as an order directing the Company to reform and improve its corporate governance and internal procedures to comply with applicable laws, attorneys' fees, and other costs.

The Company denies any allegations of wrongdoing and intends to vigorously defend against these lawsuits. The Company is unable, however, to predict the outcome of these matters at this time. Moreover, any conclusion of these matters in a manner adverse to the Company and for which it incurs substantial costs or damages not covered by the Company's directors' and officers' liability insurance would have a material adverse effect on its financial condition and business. In addition, the litigation could adversely impact the Company's reputation and divert management's attention and resources from other priorities, including the execution of business plans and strategies that are important to the Company's ability to grow its business, any of which could have a material adverse effect on the Company's business.

On May 30, 2017, a shareholder derivative action was filed against the members of the Company's Board of Directors in the United States District Court for the Southern District of New York, captioned Etelmendorf v. Bolte, et al., No. 1:17-cv-04042. The complaint alleged that defendants breached their fiduciary duties to the Company by causing or permitting the Company to make allegedly false and/or misleading statements concerning the prospects of the Company's Phase 3 trials for Fovista in combination with anti-VEGF agents for the treatment of wet AMD, and by approving certain executive compensation. The complaint also alleged that defendants were unjustly enriched as a result of the alleged conduct. The complaint purported to seek unspecified damages on behalf of the Company, as well as an order directing the Company to reform and comply with its governance obligations, attorneys' fees, and other costs. The defendants moved to dismiss the action in its entirety. Rather than oppose the motion to dismiss, on October 17, 2017, the plaintiff filed a notice of voluntary dismissal without prejudice for this action.

11. Stock Option and Compensation Plans

The Company adopted its 2007 Stock Incentive Plan (the "2007 Plan") for employees, non-employee directors and consultants for the purpose of advancing the interests of the Company's stockholders by enhancing its ability to attract, retain and motivate persons who are expected to make important contributions to the Company. The 2007 Plan provided for the granting of stock option awards, RSUs, and other stock-based and cash-based awards. Following the effectiveness of the 2013 Stock Incentive Plan described below in connection with the closing of the Company's initial public offering, the Company is no longer granting additional awards under the 2007 Plan.

In August 2013, the Company's board of directors adopted and the Company's stockholders approved the 2013 stock incentive plan (the "2013 Plan"), which became effective immediately prior to the closing of the Company's initial public offering. In June 2015, the Company's board of directors adopted a first amendment to the 2013 Plan. The 2013 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, RSUs, restricted stock awards and other stock-based awards. Upon the effectiveness of the 2013 Plan, the number of shares of the Company's common stock that were reserved for issuance under the 2013 Plan was the sum of (1) such number of shares (up to approximately 3,359,641 shares) as is equal to the sum of 739,317 shares (the number of shares of the common stock then available for issuance under the 2007 Plan), and such number of shares of the Company's common stock that are subject to outstanding awards under the 2007 Plan that expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right plus (2) an annual increase, to be added the first business day of each fiscal year, beginning with the fiscal year ending December 31, 2014 and continuing until, and including, the fiscal year ending December 31, 2023, equal to the lowest of 2,542,372 shares of the Company's common stock, 4% of the number of shares of the Company's common stock outstanding on the first day of the fiscal year and an amount determined by its board of directors. The Company's employees, officers, directors, consultants and advisors are eligible to receive awards under the 2013 Plan. However, incentive stock options may only be granted to employees of the Company.

Annual increases under the evergreen provisions of the 2013 Plan have resulted in the addition of an aggregate of approximately 6,898,000 additional shares to the 2013 Plan, including for 2018, an increase of approximately 1,444,000 shares, or 4% of the total number of shares of the Company's common stock outstanding as of January 1, 2018. As of December 31, 2017, the Company had approximately 492,000 shares available for grant under the 2013 Plan.

In April 2016, the board of directors adopted the ESPP pursuant to which the Company may sell up to an aggregate of 1,000,000 shares of common stock. The ESPP was approved by the Company's stockholders in June 2016. The ESPP allows eligible employees to purchase common stock at a price per share equal to 85% of the lower of the fair market value of the common stock at the beginning or end of each six month offering period during the term of the ESPP. The first offering period began in September 2016.

A summary of the stock option activity, weighted average exercise prices, options outstanding and exercisable as of December 31, 2017, 2016 and 2015 is as follows (in thousands except weighted average exercise price):

	Years ended December 31,					
	2017		2016		2015	
	Common Stock Options	Weighted Average Exercise Price	Common Stock Options	Weighted Average Exercise Price	Common Stock Options	Weighted Average Exercise Price
Outstanding, December 31, 2016	3,359	$ 39.92	3,009	$ 30.43	3,680	$ 21.03
Granted	3,024	$ 3.50	972	$ 60.40	764	$ 47.31
Exercised	(20)	$ 1.64	(428)	$ 15.73	(1,133)	$ 10.31
Expired or forfeited	(1,079)	$ 38.17	(194)	$ 48.63	(302)	$ 34.09
Outstanding, December 31, 2017	5,284	$ 19.58	3,359	$ 39.92	3,009	$ 30.43

	Years ended December 31,		
	2017	2016	2015
Options exercisable at December 31, 2017	1,954	1,531	955
Weighted average grant date fair value (per share) of options granted during the period	$ 2.45	$ 38.18	$ 31.33

As of December 31, 2017, there were approximately 4,801,000 options outstanding, net of estimated forfeitures, that had vested or are expected to vest. The weighted-average exercise price of these options was $20.47 per option; the weighted-average remaining contractual life of these options was 8.1 years; and the aggregate intrinsic value of these options was approximately $0.4 million. A summary of the stock options outstanding and exercisable as of December 31, 2017 is as follows (in thousands except exercise prices and weighted average exercise price):

	December 31, 2017				
		Options Outstanding		Options Exercisable	
Range of Exercise Prices	Total Options Outstanding	Weighted Average Remaining Life (Years)	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price
$0.12-$10.03	3,054	9.3	$ 3.68	210	$ 6.62
$10.04-$20.00	204	5.5	$ 13.52	147	$ 13.63
$20.01-$30.00	127	5.9	$ 25.13	127	$ 25.13
$30.01-$40.00	831	5.5	$ 32.81	808	$ 32.82
$40.01-$55.00	708	7.5	$ 46.40	467	$ 46.13
$55.01-$73.22	360	8.0	$ 72.63	194	$ 72.13
	5,284	8.2	$ 19.58	1,953	$ 35.15
Aggregate Intrinsic Value	$ 492			$ 122	

Cash proceeds from, and the aggregate intrinsic value of, stock options exercised during the years ended December 31, 2017, 2016 and 2015, respectively, were as follows:

	Years ended December 31,		
	2017	2016	2015
Cash proceeds from options exercised	$ 33	$ 6,934	$ 11,473
Aggregate intrinsic value of options exercised	$ 43	$ 14,439	$ 49,255

In connection with stock option awards granted to employees, the Company recognized approximately $13.1 million, $22.8 million and $15.5 million in share-based compensation expense during the years ended December 31, 2017, 2016 and 2015, respectively, net of expected forfeitures. As of December 31, 2017, there were approximately $14.8 million of unrecognized compensation costs, net of estimated forfeitures, related to stock option awards granted to employees, which are expected to be recognized over a remaining weighted average period of 2.5 years.

In connection with stock option awards granted to consultants, the Company recognized approximately $0.3 million, $1.7 million and $4.1 million in share-based compensation expense during the years ended December 31, 2017, 2016 and 2015, respectively, net of expected forfeitures. As of December 31, 2017, there were approximately $0.2 million of unrecognized compensation costs, net of estimated forfeitures, related to stock option awards granted to consultants, which are expected to be recognized over a remaining weighted average period of 1.8 years.

The following table presents a summary of the Company's outstanding RSU awards granted as of December 31, 2017 (in thousands except weighted average grant-date fair value):

	Restricted Stock Units	Weighted Average Grant-Date Fair Value
Outstanding, December 31, 2016	721	$ 55.33
Awarded	249	$ 4.42
Vested	(341)	$ 20.15
Forfeited	(302)	$ 50.30
Outstanding, December 31, 2017	327	$ 51.08

As of December 31, 2017, there were approximately 187,000 RSUs outstanding, net of estimated forfeitures, that are expected to vest. The weighted-average fair value of these RSUs was $47.25 per share; and the aggregate intrinsic value of these RSUs was approximately $0.6 million.

In connection with RSUs granted to employees, the Company recognized approximately $4.4 million, $6.9 million and $5.2 million in share-based compensation expense during the years ended December 31, 2017, 2016 and 2015, respectively, net of expected forfeitures. As of December 31, 2017, there was approximately $5.6 million of unrecognized compensation costs, net of estimated forfeitures, related to RSUs granted to employees, which are expected to be recognized over a remaining weighted average period of 2.0 years. The total fair value of the RSUs that vested during the year ended December 31, 2017 was $7.5 million.

In connection with RSUs granted to consultants, the Company recognized approximately $0.3 million in share-based compensation expense during the year ended December 31, 2017, net of expected forfeitures. There were no RSUs granted to consultants during the year ended December 31, 2016. As of December 31, 2017, there were approximately $0.1 million of unrecognized compensation costs, net of estimated forfeitures, related to RSUs granted to consultants, which are expected to be recognized over a remaining weighted average period of 1.7 years.

In connection with the ESPP made available to employees, the Company recognized a $0.1 million amount of share-based compensation expense during the years ended December 31, 2017 and December 31, 2016, respectively, net of expected forfeitures. As of December 31, 2017, there was a de minimis amount of unrecognized compensation costs, net of estimated forfeitures, related to the ESPP, which are expected to be recognized over 0.3 years. There were 16,358 shares of common stock issued under the ESPP during the year ended December 31, 2017. Cash proceeds from ESPP purchases were $38 thousand during the year ended December 31, 2017. There were no shares of common stock issued under the ESPP plan during the year ended December 31, 2016, as the first offering period under the ESPP commenced in September 2016. As of December 31, 2017, 983,642 shares were available for future purchases under the ESPP.

12. Employee Benefit Plan

The Company maintains a defined contribution 401(k) plan available to employees. Employee contributions are voluntary and are determined on an individual basis, limited by the maximum amounts allowable under federal tax regulations. The Company's matching contributions to employees totaled approximately $0.7 million, $0.8 million and $0.5 million during the years ended December 31, 2017, 2016 and 2015, respectively.

13. Fair Value Measurements

ASC 820, *Fair Value Measurements and Disclosures*, defines fair value as the price that would be received to sell an asset, or paid to transfer a liability, in the principal or most advantageous market in an orderly transaction between market participants on the measurement date. The fair value standard also establishes a three-level hierarchy, which requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value.

The Company reviews investments on a periodic basis for other than temporary impairments. This review is subjective as it requires management to evaluate whether an event or change in circumstances has occurred in the period that may have a significant adverse effect on the fair value of the investment. The Company uses the market approach to measure fair value for its financial assets. The market approach uses prices and other relevant information generated by market transactions involving identical or comparable assets. The Company classifies its corporate debt securities within the fair value hierarchy as Level 2 assets, as it primarily utilizes quoted market prices or rates for similar instruments to value these securities.

The valuation hierarchy is based upon the transparency of inputs to the valuation of an asset or liability on the measurement date. The three levels are defined as follows:

- Level 1—inputs to the valuation methodology are quoted prices (unadjusted) for an identical asset or liability in an active market. The Company's Level 1 assets consist of investments in money market funds and U.S. Treasury securities.
- Level 2—inputs to the valuation methodology include quoted prices for a similar asset or liability in an active market or model-derived valuations in which all significant inputs are observable for substantially the full term of the asset or liability. The Company's Level 2 assets consist of investments in investment-grade corporate debt securities.
- Level 3—inputs to the valuation methodology are unobservable and significant to the fair value measurement of the asset or liability. The Company does not hold any assets that are measured using Level 3 inputs.

The following table presents, for each of the fair value hierarchy levels required under ASC 820, the Company's assets and liabilities that are measured at fair value on a recurring basis as of December 31, 2017:

	Fair Value Measurement Using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Assets			
Investments in money market funds*	$ 162,457	$ —	$ —
Investments in U.S. Treasury securities	$ —	$ —	$ —
Investments in Corporate debt securities	$ —	$ —	$ —

The following table presents, for each of the fair value hierarchy levels required under ASC 820, the Company's assets and liabilities that are measured at fair value on a recurring basis as of December 31, 2016:

	Fair Value Measurement Using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Assets			
Investments in money market funds*	$ 108,096	$ —	$ —
Investments in U.S. Treasury securities	$ 120,261	$ —	$ —
Investments in Corporate debt securities	$ —	$ 35,087	$ —

* Investments in money market funds, U.S. Treasury securities and corporate debt securities with maturities less than 90 days are reflected in cash and cash equivalents in the accompanying Balance Sheets.

No transfer of assets between Level 1 and Level 2 of the fair value measurement hierarchy occurred during the years ended December 31, 2017 or December 31, 2016.

14. Restructuring Activities

In December 2016, the Company announced its intention to implement a reduction in personnel to focus on an updated business plan. In January 2017, the Board of Directors approved a plan to implement a reduction in personnel involving approximately 80% of the Company’s workforce based on the number of employees at the time the plan was approved. During the year ended December 31, 2017, the Company's workforce has been reduced by 122 employees in connection with the reduction in personnel and through natural attrition. The Company substantially completed the reduction in personnel during 2017. In connection with such reduction in personnel, the Company incurred approximately $13.1 million of pre-tax charges through the fourth quarter of 2017, of which approximately $12.1 million in the aggregate is expected to result in cash expenditures. These pre-tax charges relate to (a) severance, stock compensation and other employee costs of approximately $11.0 million and (b) lease termination costs of approximately $2.1 million. As of December 31, 2017, the Company's cash expenditures related to such reduction in personnel totaled $9.6 million.

In connection with the reduction in personnel, the Company recognized approximately $11.0 million of severance, stock compensation and other employee costs for the year ended December 31, 2017, of which $7.5 million was recorded in "Research and development" expense and $3.5 million were recorded in "General and administrative" expense in the Company's Statements of Operations.

As of December 31, 2017, the Company's accrual balance for severance and benefit costs was $2.5 million which was recorded in "Accounts payable and accrued expenses" in the Company's Balance Sheet. The severance and other employee cost accruals as of December 31, 2017 are expected to be paid through to December of 2018.

The following is a reconciliation of the severance-related accrual activity for the year ended December 31, 2017:

	Accrued Severance and Other Employee Costs
Beginning Balance	$ —
Accrued restructuring expenses	12,105
Payments	(9,576)
Ending Balance	$ 2,529

In January 2017, the Company issued a notice of termination under the Lease Agreement, dated as of September 30, 2007, between the Company and One Penn Plaza LLC, as previously supplemented and amended (as so supplemented and amended, the “Lease”) for office space at One Penn Plaza in New York, New York. The termination of the Lease triggered an early termination payment by the Company of approximately $0.9 million. On November 1, 2017, the Company and One Penn

Plaza LLC executed a further amendment to the Lease. Payments under the further lease amendment will not constitute restructuring charges.

On January 26, 2017, the Company issued a notice of termination under the Sublease Agreement between the Company and Otsuka America Pharmaceutical, Inc. (the “Sublease”) for office space at One University Square, Princeton, New Jersey. The termination of the Sublease triggered an early termination payment by the Company of approximately $1.2 million.

On January 26, 2017, the Company issued a notice of termination under its Office Lease Agreement between the Company and PSN Partners, L.P. (the “Office Lease”) for office space in Palmer Square in Princeton, New Jersey. The termination of the Office Lease did not trigger any early termination payment.

During January 2017, the Company made the early termination payments as described above and recognized $2.1 million of additional facilities costs which were recorded in "General and administrative" expense in the Company's Statements of Operations.

15. Selected Quarterly Financial Information (unaudited)

The following is a summary of the quarterly results of operations for the years ended December 31, 2017 and 2016:

	2017			
	March 31	June 30	September 30	December 31
Collaboration revenue	$ 1,662	$ 1,661	$ 206,654	$ —
Research and development expenses	31,979	15,657	10,707	7,946
General and administrative expenses	13,159	8,552	7,059	6,913
Income (loss) from operations	(43,476)	(22,548)	188,888	(14,859)
Net income (loss) attributable to common stockholders	$ (43,122)	$ (22,204)	$ 189,073	$ (9,542)
Basic earnings (loss) per common share	$ (1.20)	$ (0.62)	$ 5.26	$ (0.26)
Diluted earnings (loss) per common share	$ (1.20)	$ (0.62)	$ 5.25	$ (0.26)

	2016			
	March 31	June 30	September 30	December 31
Collaboration revenue	$ 15,721	$ 28,198	$ 1,668	$ 5,322
Research and development expenses	37,770	48,262	50,854	59,409
General and administrative expenses	14,696	10,489	12,024	12,968
Loss from operations	(36,745)	(30,553)	(61,210)	(67,055)
Net loss attributable to common stockholders	$ (36,301)	$ (29,945)	$ (60,891)	$ (66,283)
Basic and diluted loss per common share	$ (1.03)	$ (0.85)	$ (1.71)	$ (1.86)

FIFTH AMENDMENT OF LEASE

THIS FIFTH AMENDMENT OF LEASE, made as of the 1st day of October, 2017 (this "Amendment"), by and between ONE PENN PLAZA LLC, a New York limited liability company, having an office c/o Vornado Office Management LLC, 888 Seventh Avenue, New York, New York 10019 ("Landlord"), and OPHTHOTECH CORPORATION, a Delaware corporation, having an office at One Penn Plaza, New York, New York 10019 ("Tenant").

W I T N E S S E T H:

WHEREAS, by Lease, dated as of September 30, 2007 (the "Original Lease"), between Landlord and Tenant, Landlord did demise and lease to Tenant and Tenant did hire and take from Landlord, a portion of the rentable area located on the thirty-fifth (35th) floor of the building known as and by the street address of One Penn Plaza, New York, New York (the "Building"), as more particularly described therein (the "Original Premises");

WHEREAS, the Original Lease was amended and modified by a letter agreement, dated as of September 28, 2012 (the "Letter Agreement"), between Landlord and Tenant;

WHEREAS, by Amendment of Lease, dated as of August 30, 2013 (the "First Amendment"), (x) Tenant surrendered the Original Premises to Landlord, (y) Landlord did demise and lease to Tenant and Tenant did hire and take from Landlord, a portion of the nineteenth (19th) floor of the Building, as more particularly described therein (the "First 19th Floor Premises"), and (z) Landlord and Tenant extended the term of the Original Lease;

WHEREAS, by Second Amendment of Lease, dated as of December 20, 2013 (the "Second Amendment"), Landlord did demise and lease to Tenant and Tenant did hire and

take from Landlord, an additional portion of the nineteenth (19th) floor of the Building, as more particularly described therein (the "Second 19th Floor Premises");

WHEREAS, by Third Amendment of Lease, dated as of April 18, 2014 (the "Third Amendment"), Landlord did demise and lease to Tenant and Tenant did hire and take from Landlord an additional portion of the nineteenth (19th) floor of the Building, as more particularly described therein (the "Third 19th Floor Premises");

WHEREAS, by Fourth Amendment of Lease, dated as of December 31, 2014 (the "Fourth Amendment"), Landlord did demise and lease to Tenant and Tenant did hire and take from Landlord an additional portion of the nineteenth (19th) floor of the Building, as more particularly described therein (the "Fourth 19th Floor Premises"; the First 19th Floor Premises, the Second 19th Floor Premises, the Third 19th Floor Premises and the Fourth 19th Floor Premises, collectively, the "Surrender Premises");

WHEREAS, by notice from Tenant to Landlord dated January 26, 2017 (the "Termination Notice"), Tenant exercised Tenant's Termination Right (as such term is defined in the Lease) with respect to the Lease; the Original Lease, as modified by the Letter Agreement, the First Amendment, the Second Amendment, the Third Amendment, the Fourth Amendment, and such notice exercising Tenant's Termination Right, the "Lease"); and

WHEREAS, Landlord and Tenant desire to terminate the Lease with respect to the Surrender Premises only and Landlord desires to lease to Tenant and Tenant desires to lease from Landlord a portion of the thirty-fifth (35^{th}) floor of the Building, as more particularly shown on the floor plan attached hereto as Exhibit "A" and made a part hereof (the "35^{th} Floor Premises") currently leased to a third party ("Existing Tenant") and to otherwise modify the Lease as set forth herein.

NOW, THEREFORE, in consideration of the mutual covenants contained herein, and for other good and valuable consideration, the mutual receipt and legal sufficiency of which are hereby acknowledged, the parties hereto, for themselves, their legal representatives, successors and assigns, hereby agree as follows:

1. Definitions. All capitalized terms used herein shall have the meanings ascribed to them in the Lease, unless otherwise defined herein.

2. Surrender.

(A) On the later to occur of (i) the 35th Floor Premises Commencement Date (as hereinafter defined) and (ii) January 31, 2018 (such later date, the "Surrender Date"), Tenant shall vacate, quit and surrender to Landlord possession of the Surrender Premises, vacant, broom clean, free of all liens, encumbrances, tenancies and occupancies by, through and under Tenant, with (subject to the penultimate sentence of this Paragraph 2(A)) all of Tenant's Property and any property of any subtenant or other occupant removed therefrom and otherwise in the condition required by the Lease, as if the Surrender Date were the Expiration Date set forth in the Lease with respect to the Surrender Premises only, and, to the intent and purpose that the term of the Lease with respect to the Surrender Premises only, be wholly merged and extinguished effective as of the Surrender Date, Tenant hereby gives, grants and surrenders all of its right, title and interest in, to and under the Lease with respect to the Surrender Premises only, to Landlord. If possession of the Surrender Premises is not surrendered to Landlord on or prior to the Surrender Date, the provisions of Article 24 of the Lease shall be applicable to such holdover by Tenant; provided, however, Tenant shall be obligated for per diem Fixed Rent only for the first three (3) days of any such holdover following the Surrender Date. Nothing contained in this Paragraph 2(A) shall permit

Tenant to retain possession of the Surrender Premises or limit in any manner Landlord's right to regain possession of the Surrender Premises, through summary proceedings or otherwise. Notwithstanding any provision herein or in the Lease to the contrary, Landlord acknowledges and agrees that (a) Tenant has no obligation of any kind to remove or restore any Alterations within the Surrender Premises and (b) Tenant at its option may, but has no obligation of any kind to, remove any of its furniture, conduit and wiring from the Surrender Premises. The provisions of this Paragraph 2(A) shall survive the surrender of the Surrender Premises and the Surrender Date.

(B) Tenant covenants, represents and warrants to Landlord that (i) Tenant is the sole and present tenant under the Lease and Tenant has not assigned, conveyed, encumbered, pledged, sublet or otherwise transferred, in whole or in part, its interest in the Lease or the Surrender Premises, nor shall Tenant do any of the foregoing prior to the Surrender Date, (ii) there are no persons or entities claiming under Tenant, or who or which may claim under Tenant, any rights with respect to the Surrender Premises, nor shall Tenant permit any such claim to arise prior to the Surrender Date, (iii) Tenant has the right, power and authority to execute and deliver this Amendment and to perform Tenant's obligations hereunder and (iv) this Amendment is a valid and binding obligation of Tenant enforceable against Tenant in accordance with the terms hereof. The foregoing covenants, representations and warranties shall survive the surrender of the Surrender Premises and the Surrender Date.

(C) Subject to the terms of Paragraph 2(A) hereof, (x) any and all provisions of the Lease which impose obligations on Tenant to pay Fixed Rent and Escalation Rent with respect to the Surrender Premises only arising from and after the Surrender Date, shall cease as of the Surrender Date**;** provided, however, that such payments shall be apportioned as of such

date, and the obligation to pay any such amounts accruing prior to the Surrender Date shall survive the surrender of the Surrender Premises and the Surrender Date, (y) any and all provisions of the Lease which impose obligations on Tenant to pay any other items of Rental with respect to the Surrender Premises only arising from and after the Surrender Date, shall cease as of the Surrender Date; provided, however, that such payments shall be apportioned as of such date, and the obligation to pay any such amounts accruing prior to the Surrender Date shall survive the surrender of the Surrender Premises and the Surrender Date, and (z) any and all other provisions of the Lease which impose obligations on Tenant with respect to the Surrender Premises only, shall cease as of the Surrender Date. Nothing contained herein shall be deemed to relieve Tenant from Tenant's obligation to pay Rental with respect to the 35th Floor Premises as set forth in Paragraph 5(A) hereof.

(D) Provided that Landlord has substantially complied with all of the terms and conditions of this Amendment (other than those obligations which by the terms of this Amendment are to be performed after the Surrender Date), effective as of the Surrender Date, Tenant hereby releases and relieves Landlord and its successors and assigns from and against any and all actions, causes of action, suits, controversies, damages, judgments, claims and demands whatsoever, at law or in equity, of every kind and nature whatsoever arising out of, or in connection with, the Surrender Premises or the Lease with respect to the Surrender Premises only. Notwithstanding the foregoing, Landlord shall not be released from any covenant, representation or warranty contained in Lease that is specifically stated to survive the Surrender Date, the surrender of the Surrender Premises, or the Expiration Date or, with respect to periods prior to the Surrender Date, any reimbursements or repayments for overcharges of Escalation Rent and electricity charges or other amounts for which Tenant is entitled to reimbursement or payment under the Lease.

(E) Provided that Tenant has substantially complied with all of the terms and conditions of this Amendment (other than those obligations which by the terms of this Amendment are to be performed after the Surrender Date), Landlord, on the Surrender Date, shall accept Tenant's surrender of the Surrender Premises and, effective as of the Surrender Date, except as otherwise set forth in this Amendment, hereby releases and relieves Tenant and its respective successors and assigns from and against all claims, obligations and liabilities of every kind and nature whatsoever thereafter arising out of or in connection with the Surrender Premises and the Lease with respect to the Surrender Premises only, relating to the period from and after the Surrender Date. Notwithstanding the foregoing, Tenant shall not be released from any covenant, representation or warranty contained in this Amendment and the Lease, which by the terms of this Amendment or the Lease is specifically stated to survive the Surrender Date, the surrender of the Surrender Premises, or the Expiration Date.

(F) Landlord and Tenant, each upon request of the other party, at any time and from time to time hereafter and without further consideration, shall execute, acknowledge and deliver to the other any instruments or documents, or take such further action, as shall be reasonably requested or as may be necessary to more effectively assure vacating, quitting and surrender of the Surrender Premises and the full benefits intended to be created by this Amendment.

3. Lease Term. The Term with respect to the 35th Floor Premises only is hereby extended on all of the same terms and conditions set forth in the Lease, as hereinafter modified (and for avoidance of doubt, subject to the terms of this Amendment, the termination of the Lease pursuant to the Termination Notice is hereby rescinded), so that the Term shall expire at 11:59 PM on December 31, 2018 (the "Extended Expiration Date"), unless it shall sooner expire pursuant to any of the terms, covenants or conditions of the Lease, as amended by this Amendment, or pursuant

to law. Accordingly, the Extended Expiration Date shall be deemed the Fixed Expiration Date, with respect to the 35th Floor Premises only, for all purposes of the Lease, as amended by this Amendment.

4. 35th Floor Premises.

From and after the date on which Landlord delivers vacant and exclusive possession of the 35th Floor Premises to Tenant, broom clean and free of all tenancies and occupancies, with Landlord's 35th Floor Premises Work (as hereinafter defined) Substantially Complete (such date, the "35th Floor Premises Commencement Date"), Landlord leases to Tenant, and Tenant hires from Landlord, the 35th Floor Premises upon all of the same terms, covenants and conditions set forth in the Lease, except as modified and amended herein. Landlord shall give Tenant ten (10) days' prior notice of the date on which Landlord reasonably believes Landlord's 35th Floor Premises Work shall be Substantially Complete. From and after the 35th Floor Premises Commencement Date, all references in the Lease, as amended hereby, to the Premises shall be deemed to mean the 35th Floor Premises, for all purposes of the Lease, as amended hereby.

5. Landlord's 35th Floor Premises Work.

(A) The work set forth on Exhibit "B" attached hereto and made a part hereof shall be referred to, collectively, as the "Landlord's 35th Floor Premises Work").

(B) Landlord shall perform Landlord's 35th Floor Premises Work in a good and workmanlike manner. Landlord shall perform Landlord's 35th Floor Premises Work in accordance with all applicable Requirements. Notwithstanding anything contained herein to the contrary, Tenant shall reimburse Landlord for up to Eighteen Thousand Dollars ($18,000.00) for the costs incurred by Landlord to perform Landlord's 35th Floor Premises Work comprised of

separately demising the 35th Floor Premises. Tenant shall so reimburse Landlord within thirty (30) days of Landlord’s invoice therefor together with reasonable back-up.

(C) Notwithstanding the provisions of this Paragraph 4 to the contrary, in the event that Substantial Completion of Landlord's 35th Floor Premises Work shall be delayed by reason of any Tenant 35th Floor Work Delays (as hereinafter defined), then only for purposes of determining the date on which the 35th Floor Premises Commencement Date shall occur, (x) the Substantial Completion of Landlord's 35th Floor Premises Work shall be deemed to have occurred on the date it would have otherwise been Substantially Complete but for such Tenant 35th Floor Work Delays notwithstanding that Landlord has not yet delivered possession of the 35th Floor Premises to Tenant and (y) the 35th Floor Premises Commencement Date shall be deemed to have occurred on the date the 35th Floor Premises Commencement Date would have otherwise occurred but for such Tenant 35th Floor Work Delays notwithstanding that Landlord has not yet delivered possession of the 35th Floor Premises to Tenant. Notwithstanding the foregoing, Landlord shall be obligated to Substantially Complete Landlord's 35th Floor Premises Work even if the 35th Floor Premises Commencement Date is deemed to occur prior to Substantial Completion thereof, notwithstanding the occurrence of Tenant 35th Floor Work Delays; provided, however, Landlord's obligation to so Substantially Complete Landlord's 35th Floor Premises Work shall be adjourned for periods of delay caused by Tenant 35th Floor Work Delay. The term "Tenant 35th Floor Work Delays" shall mean Tenant's acts or omissions (including, without limitation, if applicable, Tenant’s entry into the 35th Floor Premises prior to the 35th Floor Premises Commencement Date that interferes with the performance of Landlord's 35th Floor Premises Work) to the extent such acts or omissions by Tenant continue for more than

one Business Day after Tenant's receipt of the notice provided hereinbelow. Landlord shall notify Tenant after Landlord or its employees, agents or contractors have actual knowledge of a Tenant 35th Floor Work Delay (and state in reasonable detail the basis of such Tenant 35th Floor Work Delay). Any such notice may be given by Landlord to Tenant by email to david.carroll@ophthotech.com and todd.anderman@ophthotech.com. Any period of Tenant 35th Floor Work Delay shall not exceed the time period Landlord was actually delayed in the performance of the 35th Floor Premises Work as a result of such Tenant 35th Floor Work Delay and only to the extent such delay cause the 35th Floor Premises Commencement Date to be delayed, and any simultaneous Tenant 35th Floor Work Delays shall be deemed to run concurrently, not consecutively, and shall not be "double" counted.

(D) Upon Tenant's reasonable advance request therefor, which request may be made verbally to Landlord's property management team, to the extent permitted by applicable Requirements, Tenant shall be permitted to enter the 35th Floor Premises from time to time, during Landlord's performance of Landlord's 35th Floor Premises Work solely for purposes of preparing for the installation of and installing IT systems and Tenant's Property therein; it being understood, however, that (i) Tenant shall not have the right to enter the 35th Floor Premises as aforesaid unless Tenant is accompanied by a designated representative of Landlord at all times during such entry (it being agreed that Landlord shall use commercially reasonable efforts to provide a designated representative to accompany Tenant as contemplated herein), and (ii) during any period in which Tenant is in the 35th Floor Premises, (x) Tenant shall comply with all terms and conditions of the Lease, as amended hereby (and the same shall be deemed to apply during such period), other than the obligation to pay Fixed Rent and Escalation Rent with respect

to the 35th Floor Premises and (y) Tenant shall not interfere with the operation of the Building or interfere with or delay Landlord's performance of and completion of Landlord's 35th Floor Premises Work (it being understood, however, that to the extent that Landlord's 35th Floor Premises Work is delayed solely by Tenant's entry into the 35th Floor Premises and/or any such preparation or installation as aforesaid and Tenant is notified of same, the same shall constitute a Tenant 35th Floor Work Delay to the extent such conduct by Tenant continues for more than one Business Day after Tenant's receipt of such notice) .

(E) Tenant shall not be required to pay for the first ten (10) hours of Tenant's overtime use of the freight elevator only for Tenant's initial move into, and/or performance of Alterations in, the 35th Floor Premises (but not for purposes associated with the ordinary conduct of Tenant's business).

(F) All furniture, fixtures and equipment ("FF&E") in the 35th Floor Premises and more particularly set forth in Exhibit "C" attached hereto and made a part hereof shall be delivered in "as is, where is" condition. All FF&E shall be maintained by Tenant during the Term in good order and repair, subject to reasonable wear and tear and obsolescence. Tenant shall have no obligation to remove any FF&E at the end of the Term. Tenant acknowledges that Landlord makes no representations of any kind to Tenant with respect to any FF&E, or its merchantability or suitability for the use to which Tenant intends to put them.

6. Modification of Lease: 35th Floor Premises. From and after the 35th Floor Premises Commencement Date, the Lease with respect to the 35th Floor Premises only, is hereby amended and modified as follows:

(A) The Fixed Rent (together with the Electricity Inclusion Factor as the date hereof) shall be an amount equal to Six Hundred Fifty-Three Thousand Five Hundred Ninety-Four Dollars and No Cents ($653,594.00) per annum ($54,466.20 per month) for the period commencing on the 35th Floor Premises Commencement Date and ending on the Extended Expiration Date.

(B) The Rentable Area of the 35th Floor Premises shall be deemed to be thirteen thousand five hundred forty-six (13,546) square feet in the aggregate.

(C) The provisions of Article 2 of the Lease shall not be applicable with respect to the 35th Floor Premises to the effect that from and after the 35th Floor Premises Commencement Date Tenant shall not be obligated to pay Escalation Rent with respect thereto.

(D) Section 3.8 of the Lease (as set forth in the First Amendment) shall be applicable to the 35th Floor Premises, except that the Designated Shaftway shall be a shaft location reasonably designated by Landlord.

(E) Section 5.1 of the Lease (as amended by the First Amendment) shall be applicable to the 35th Floor Premises, except that references therein to the nineteenth (19th) floor of the Building shall be deemed to be references to the thirty-fifth (35th) floor of the Building.

7. Additional Modifications of Lease. From and after the date hereof, the Lease is hereby amended and modified as follows:

(A) Section 4.1(E) of the Lease is amended and modified to insert the following before the period at the end thereof: “and further provided, however, that Overtime Periods

for the HVAC System shall mean times other than the periods from 8:00 A.M. to 8:00 P.M. on Business Days and 9:00 A.M. to 1:00 P.M. on Saturdays".

(B) The term "Transfer Inflow" (as such term is defined in Section 17.6(B)(2) of the Lease) is hereby amended and modified to insert the following at the end thereof:

> "Should any amount included in the Transfer Inflow cause the Transfer Profit to fail to qualify as "rents from real property," as that term is defined in Section 856(d) of the Internal Revenue Code of 1986, as amended, the fair market value of such amount, as determined by Landlord in its sole discretion, shall be excluded from the Transfer Inflow and no Transfer Profit shall be paid to Landlord with respect to such excluded amount."

(C) Section 29.1(A) of the Lease is amended and modified to insert, before the words "Tenant shall indemnify" in the first line thereof, the words "to the fullest extent permitted by law".

(D) Section 29.2(A) of the Lease is amended and modified to insert, before the words "Landlord shall indemnify" in the first line thereof, the words "to the fullest extent permitted by law".

(E) Paragraph 12 of the Fourth Amendment is hereby deleted in its entirety.

(F) Section 27.1 of the Lease is amended and modified to have notices to Tenant given to Tenant at One Penn Plaza, New York, New York 10119, Attention: Jeanne Vautin, Suite 1924 prior to the Surrender Date and to Suite 3520 after the Surrender Date and upon the 35th Floor Premises Commencement Date, with a copy to: Todd Anderson.

8. Condition of Premises. Tenant represents that it has made a thorough inspection of the 35th Floor Premises and, subject to the terms of this Amendment, Landlord's continuing obligations under Section 8.1 of the Lease and the other applicable provisions of the Lease, the performance of the Landlord's 35th Floor Premises Work, and the continuance of the Premises in its current condition as of the date hereof without damage (except reasonable wear and tear) agrees to take the 35th Floor Premises in its "as-is" condition existing on the 35th Floor Premises Commencement Date (subject to latent defects in Landlord's 35th Floor Premises Work). Tenant further acknowledges and agrees that notwithstanding anything to the contrary contained in the Lease, as amended hereby, Landlord has made no representations with respect to the 35th Floor Premises and subject to Landlord's continuing obligations under Section 8.1 and Section 11.2 of the Lease and other applicable provisions of the Lease, Landlord shall have no obligation to perform any work (other than Landlord's 35th Floor Premises Work to provide any work allowance or rent credit, or to alter, improve, decorate, or otherwise prepare the 35th Floor Premises for Tenant's occupancy. On the 35th Floor Premises Commencement Date, the 35th Floor Premises shall be in broom clean condition. Promptly following the 35th Floor Premises Commencement Date, Landlord shall provide Tenant with an ACP-5 covering the 35th Floor Premises. Landlord hereby acknowledges and agrees that Tenant shall not be obligated to perform Alterations to comply with the Americans with Disabilities Act with respect to the 35th Floor Premises (except to the extent the need for such compliance arises from Tenant's Alterations or its manner of use) and the 35th Floor Premises shall comply with Local Law 26/04.

9. Liability of Landlord. The provisions of Section 31.4 of the Lease shall be applicable to the Lease, as modified by this Amendment. Tenant shall look solely to Landlord to

enforce Landlord's obligations under the Lease, as amended by this Amendment and shall not seek any damages against any of the member, managers, partners, shareholders, directors, officers and principals, direct and indirect, comprising Landlord (collectively, the "Parties"). The liability of Landlord for Landlord's obligations under the Lease, as amended by this Amendment, shall be limited to Landlord's interest in the Real Property and the proceeds thereof. Tenant shall not look to any property or assets of Landlord (other than Landlord's interest in the Real Property and the proceeds thereof) in seeking either to enforce Landlord's obligations under the Lease, as amended hereby or to satisfy a judgment for Landlord's failure to perform such obligations.

10. Brokerage.

(A) Tenant represents and warrants to Landlord that it has not dealt with any broker, finder or like agent in connection with this Amendment other than CBRE, Inc. ("Broker"). Tenant does hereby indemnify and hold Landlord harmless of and from any and all loss, costs, damage or expense (including, without limitation, attorneys' fees and disbursements) incurred by Landlord by reason of any claim of or liability to any broker, finder or like agent excluding Broker who shall claim to have dealt with Tenant in connection herewith.

(B) Landlord represents and warrants to Tenant that it has not dealt with any broker, finder or like agent in connection with this Amendment other than Broker. Landlord does hereby indemnify and hold Tenant harmless of and from any and all loss, costs, damage or expense (including, without limitation, attorneys' fees and disbursements) incurred by Tenant by reason of any claim of or liability to any broker, finder or like agent, excluding Broker, who shall claim to have dealt with Landlord in connection herewith.

(C) The provisions of this Paragraph 10 shall survive the expiration or termination of the Lease, as amended by this Amendment.

11. Authorization. Tenant represents and warrants to Landlord that its execution and delivery of this Amendment has been duly authorized and that the person executing this Amendment on behalf of Tenant has been duly authorized to do so, and that no other action or approval is required with respect to this transaction. Landlord represents and warrants to Tenant that its execution and delivery of this Amendment has been duly authorized and that the person executing this Amendment on behalf of Landlord has been duly authorized to do so, and that no other action or approval is required with respect to this transaction.

12. Full Force and Effect of Lease. Except as modified by this Amendment, the Lease and all covenants, agreements, terms and conditions thereof shall remain in full force and effect and are hereby in all respects ratified and confirmed.

13. Entire Agreement. The Lease, as amended by this Amendment, constitutes the entire understanding between the parties hereto with respect to the matters set forth herein and may not be changed orally but only by an agreement in writing signed by the party against whom enforcement of any waiver, change, modification or discharge is sought.

14. Enforceability. This Amendment shall not be binding upon or enforceable against either Landlord or Tenant unless, and until, Landlord and Tenant, each in its sole discretion, shall have executed and unconditionally delivered to the other an executed counterpart of this Amendment.

15. Counterparts. This Amendment may be executed in one or more counterparts each of which when taken together shall constitute but one original.

[REMAINDER OF PAGE INTENTIONALLY LEFT BLANK]

IN WITNESS WHEREOF, the parties hereto have executed this Fifth Amendment as of the date first above written.

ONE PENN PLAZA LLC, Landlord

By: Vornado Realty L.P., its managing member

By: Vornado Realty Trust, its general partner

By: /s/ David R. Greenbaum

David R. Greenbaum
President – New York Division

OPHTHOTECH CORPORATION, Tenant

By: /s/ David F. Carroll
Name:David F. Carroll
Title: CFO / SVP

TENANT'S EIN#:20-8185347

UNIFORM FORM CERTIFICATE OF ACKNOWLEDGMENT
(Within New York State)

STATE OF _____)
: ss.:
COUNTY OF _____)

On the _____ day of _____, in the year 2017, before me, the undersigned personally appeared _____, personally known to me or proved to me on the basis of satisfactory evidence to be the individual(s) whose name(s) is (are) subscribed to the within instrument and acknowledged to me that he/she/they executed the same in his/her/their capacity(ies), and that by his/her/their signature(s) on the instrument, the individual(s), or the person upon behalf of which the individual(s) acted, executed the instrument.

_____
Notary Public

UNIFORM FORM CERTIFICATE OF ACKNOWLEDGMENT
(Outside of New York State)

STATE OF New Jersey)
: ss.:
COUNTY OF Middlesex)

On the 20th day of October, in the year 2017, before me, the undersigned, personally appeared David Carroll, personally known to me or proved to me on the basis of satisfactory evidence to be the individual(s) whose name(s) is (are) subscribed to the within instrument and acknowledged to me that he/she/they executed the same in his/her/their capacity(ies), that by his/her/their signature(s) on the instrument, the individual(s), or the person upon behalf of which the individual(s) acted, executed the instrument, and that such individual made such appearance before the undersigned in the County of Middlesex. (Insert the city or other political subdivision and the state or country or other place the acknowledgment was taken.)

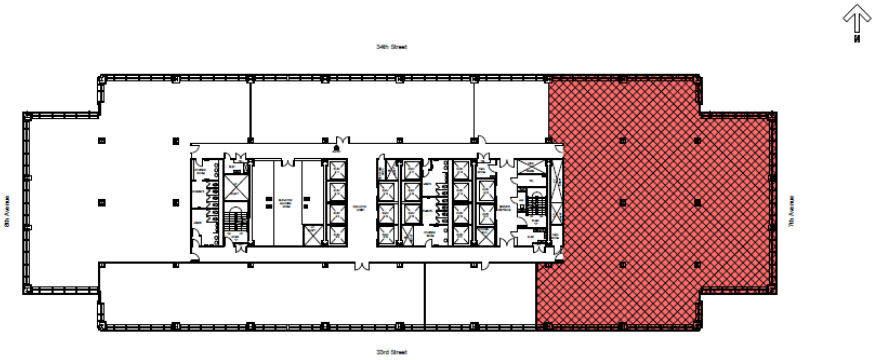
/s/ Joanne Dera, Notary

(Signature and office of individual taking acknowledgment)

Exhibit "A"

35th Floor Premises

One Penn Plaza
35th Floor



VORNADO
REALTY TRUST

Exhibit "B"

Landlord's 35th Floor Premises Work

1. Landlord shall separately demise the 35th Floor Premises in accordance with the plan attached hereto as Exhibit "A"
2. Landlord shall steam clean the carpets in the 35th Floor Premises

Exhibit "C"

FF&E

1. Chairs: 19
2. Conference room tables: 2
3. Cubicles: 29
4. Guest Tables (in private offices): 3
5. Desks w/ overhead cabinets (private offices): 16
6. TV’s w/ projector: 2
7. Credenzas: 3
8. Refrigerator: 1
9. Water filters/coolers: 2
10. Microwaves: 2
11. Storage Shelves: 3
12. File Cabinets: 5 gray, 1 black, 6 silver
13. IT Racks: 1

Exhibit 10.22

OPHTHOTECH
One Penn Plaza, 35th Floor, New York, NY 10119
Phone: 212-845-8200 Fax: 212-845-8250

January 5, 2018

Ms. Barbara A. Wood

Re: Separation Agreement and General Release

Dear Barbara:

This letter agreement (the "Letter Agreement") confirms our agreement concerning your separation from Ophthotech Corporation ("Ophthotech" or the "Company"). Subject to the terms of this Letter Agreement, your employment will end effective on the earliest of (i) March 31, 2018, (ii) such date as may be mutually agreed between you and the Company, and (iii) such date as the Company terminates your employment for Cause, as that term is defined in the February 20, 2015 severance benefits agreement between you and the Company (the "Severance Agreement") (as applicable, the "Separation Date"). By signing a copy of this Letter Agreement in the space provided below, you agree to the terms and conditions set forth herein.

A. **Transition Period**. The period between the Agreement Effective Date (as defined in Paragraph F.5 below) and the Separation Date will be a transition period (the "Transition Period"), during which you will continue to work on a full-time basis, and, at the direction of the Company, assist as requested and in a timely, professional and cooperative manner with transitioning your duties and responsibilities. During the Transition Period, you will continue to receive your current base salary and may continue to participate in the Company's benefit plans to the extent you remain eligible (and pursuant to the terms and conditions of such plans). In the event the Company terminates your employment for Cause, you will not be eligible to receive the payments and benefits described in Paragraph B of this Letter Agreement, nor will you receive any further salary payments, benefits, or other compensation from the Company following your termination from employment, except as and to the extent required by law.

B. **The Company's Obligations**. In exchange for your (a) timely execution and return (as set forth in Paragraph F.6 below), and non-revocation, of this Letter Agreement, (b) compliance with the terms of this Letter Agreement, and (c) timely execution and return (as set forth in Paragraph F.6 below), and non-revocation, of the Reaffirmation of Letter Agreement attached as Exhibit A (the "Reaffirmation"), the Company will, provided you remain eligible pursuant to Paragraph A above, provide you with the following payments and benefits:

1. Pursuant to their terms, any stock option and restricted stock unit awards granted to you by the Company that are unvested as of the Separation Date will terminate effective as of such date. If you execute and do not revoke the Reaffirmation, then immediately following the Reaffirmation Effective Date (as defined in Paragraph F.6 below), the exercise period for your outstanding stock options will be extended such that the stock options in which you have vested as of the Separation Date will remain exercisable for a period of one year following the Separation Date (but in no event shall such exercise period be extended to later than the final exercise date (as described in any applicable agreement governing the stock option award). You understand that any option subject to this extended exercise period shall cease to be treated for tax purposes as an incentive stock option effective as of the date hereof.

2. The Company will provide you with a severance payment ("Severance Payment"). The Severance Payment shall consist of:

    i. a lump sum payment in the amount of $404,620, consisting of twelve (12) months of your current base salary; and

    ii. a lump sum payment in an amount equal to the pro-rated portion, as of the Separation Date, of your Target Bonus (as such term is defined in the Severance Agreement).

    Section 4(a) of the Severance Agreement (Code Section 409A) shall govern any payment under this Letter Agreement.

    Except as provided for in this Paragraph B.2, both the Severance Agreement and the letter outlining the terms of your offer of employment with the Company dated October 21, 2013 and revised October 22, 2013 (the "Offer Letter") are of no further force or effect.

3. Your group medical and dental coverage will continue through the last date of the month in which your Separation Date occurs. You will be given separate information regarding your right to continue your group health/dental/vision coverage, as required by the Consolidated Omnibus Budget Reconciliation Act of 1985 ("COBRA"). All COBRA rights are subject to your completion and submission of the proper forms in the times allotted.

    Provided you timely elect COBRA continuation coverage, the Company will reimburse you for the monthly premium to continue such coverage for the lesser of (i) the twelve (12) full calendar months immediately following the last day of the calendar month in which your Separation Date occurs; and (ii) the end of the calendar month in which you become eligible to receive group health plan coverage under another employee benefit plan. For the avoidance of doubt, such reimbursement of monthly premiums shall be subject to Section 4(a) of the Severance Agreement (Code Section 409A).

4. The Company will allow you to retain the cellphone that the Company previously provided to you in connection with your employment (the "Cellphone"), provided that following the Separation Date you will need to immediately transfer the telephone number to your own mobile service, as the Company will not continue to pay for service following the Separation Date. Notwithstanding the foregoing, you acknowledge and agree that you must return the Cellphone to the Company immediately if you revoke this Letter Agreement, or if you do not timely sign and return the Reaffirmation, or if you revoke the Reaffirmation.

5. All payments under this Letter Agreement will be subject to all deductions required by law, including applicable taxes and withholdings. The Severance Payment will be made in one lump sum in accordance with the Company's normal payroll practices, no later than the second regular payroll date following the Reaffirmation Effective Date. In accordance with its normal payroll practices, the Company will mail to the address listed above (or such other address as you have provided in writing to the Company's Human Resources Department) an IRS Form W-2 (a) following the end of 2018, covering compensation you received in 2018, inclusive of the Severance Payment and any COBRA reimbursement payments received in 2018 and (b) following the end of 2019, covering any COBRA reimbursement payments received in 2019.

C. **Your Obligations**. In exchange for the consideration set forth in this Letter Agreement, including without limitation the Company providing you with the payments and benefits described in Paragraph B, above, to which you are not otherwise entitled, you voluntarily agree to the following:

1. You, for yourself and for your heirs, executors, administrators, successors and assigns (referred to collectively as "Releasor"), forever release and discharge the Company and any and all of the Company's past and present affiliates, parent entities, subsidiaries, divisions, offices, branches, assets, employee benefit plans, funds, investment funds, successors and assigns, and any and all of its and their past and present officers, directors, partners, members, shareholders, agents, attorneys, employees, agents, trustees, fiduciaries, representatives, administrators, successors and assigns (whether acting in such capacity or otherwise) (referred to collectively as the "Releasees"), from any and all claims, demands, causes of action, fees and liabilities of any kind whatsoever, whether known or unknown, which Releasor ever had, now has or may have against Releasees or any of them by reason of any actual or alleged act, omission, transaction, practice, conduct, occurrence or other matter from the beginning of the world up to and including the date you sign this Letter Agreement based on your employment with the Company and the termination of your employment (other than claims you may have based upon your rights under this Letter Agreement).

2. Without limiting the generality of the foregoing general release, by signing this Letter Agreement you agree that you are releasing Releasees from any and all claims arising

out of your employment with the Company, the terms and conditions of such employment and/or the termination of such employment, including but not limited to: (i) any claim under the Employee Retirement Income Security Act of 1974 ("ERISA"), Title VII of the Civil Rights Act of 1964, the Civil Rights Act of 1991, the Civil Rights Act of 1866, the Age Discrimination in Employment Act (including the Older Workers Benefit Protection Act), the Equal Pay Act, the Americans with Disabilities Act, the Family and Medical Leave Act, the National Labor Relations Act, the Sarbanes-Oxley Act, the Dodd-Frank Act, the New York State Human Rights Law, the New York City Human Rights Law, the New York Labor Law (all as amended), and any other applicable federal, state or local statute; (ii) any other claim of discrimination, harassment or retaliation in employment (whether based on federal, state or local law, statutory or decisional); (iii) any claim sounding in tort, common law or contract (express or implied)(including without limitation any claims under the Severance Agreement or the Offer Letter), wrongful discharge, whistleblowing, detrimental reliance, or defamation; (iv) any claim based on the Stock Grants; and (v) any claim for attorney's fees, costs, disbursements, emotional distress, compensatory and/or punitive damages and/or the like.

3. You acknowledge that you may hereafter discover claims or facts in addition to or different from those which you now know or believe to exist with respect to the subject matter of this Letter Agreement and which, if known or suspected at the time you execute this Letter Agreement, may have materially affected this Letter Agreement and your decision to enter into it. Nevertheless, you hereby waive any right, claim or cause of action that might arise as a result of such different or additional claims or facts.

4. You represent and warrant that, except as otherwise permitted below, you have maintained in the strictest confidence all information relating to the Company and/or the Releasees and their respective business that is not generally known by persons not employed by the Company and that could not easily be determined or learned by someone outside of the Company. All of the foregoing shall be deemed "Confidential Information." You agree that you will maintain in the strictest confidence all Confidential Information, except as set forth below. In addition, you hereby acknowledge and affirm your post-termination obligations under the Invention, Non-Disclosure, Non-Competition and Non-Solicitation Agreement between you and the Company dated October 23, 2013 (the "Covenant Agreement"), which are expressly incorporated herein. Notwithstanding the foregoing, however, nothing in the Covenant Agreement, this Letter Agreement or elsewhere shall be interpreted to (i) restrict your ability, after you cease to be an employee of the Company, to practice law, in violation of New York Rule of Professional Conduct 5.6 or other applicable rules of professional conduct; or (y) expand the scope of your duty to maintain privileged or confidential information obtained in connection with the your role as counsel for the Company beyond what is permitted under New York Rules of Professional Conduct 1.6 and 1.9, or other applicable rules of professional conduct.

5. You agree that you have not and in the future will not, except as otherwise permitted below, disclose to any other person or entity (directly or indirectly), Confidential Information, except (a) as may be required pursuant to a valid subpoena, a request by a government agency (including but not limited to the United States Equal Employment Opportunity Commission ("EEOC") or the Securities and Exchange Commission ("SEC")) in connection with any charge filed, investigation or proceeding or as otherwise required by law; and (b) to your immediate family members, financial advisors and attorneys, provided that you first inform them of the confidentiality of this Letter Agreement and they agree to maintain its confidentiality. You further agree that you will not solicit or initiate any demand or request by others for the disclosure of Confidential Information; or encourage or induce any other person to make any statement or disclosure of Confidential Information. In the event that you receive an inquiry from the press or otherwise that could potentially call for the disclosure of Confidential Information, you will respond to the inquiry, if at all, by stating "I cannot comment," or words to that effect.

6. To the extent permitted by law, you will cooperate fully with the Company, and provide assistance to the Company, in connection with (a) the orderly transition of all of your responsibilities and matters, (b) any pending or future litigation, administrative proceeding, or investigatory matter, and (c) any other matters for which you were responsible or with respect to which your knowledge may be of assistance to the Company. You further agree that, in the event you are subpoenaed by any person or entity to give testimony (in a deposition, court proceeding or otherwise) which in any way relates to your employment with the Company, you will give prompt written notice of such request (other than in the event of a subpoena issued by a government agency) to the Company's Head of Human Resources, at the address above to allow the Company a reasonable opportunity to first contest the right of the requesting person or entity to such disclosure. Nothing in this Letter Agreement shall preclude you from responding truthfully to a valid subpoena. You agree to provide such cooperation and assistance as requested by the Company, subject to the reasonable efforts of the Company to accommodate any new employment obligations you may have, and the Company shall reimburse you for your reasonable out-of-pocket expenses in connection therewith. For the avoidance of doubt, nothing in this Paragraph or elsewhere in the Agreement is intended in any way to prevent you from testifying fully and truthfully in any action or proceeding or in connection with any regulatory matter.

7. You agree that you have not and will not, except as otherwise permitted below, make any disparaging, critical or otherwise detrimental statements (orally or in writing) to any person or entity concerning the Company, its officers, directors, managing members, investors, employees, attorneys, representatives, affiliates, customers, clients, its and their business affairs or financial condition, the circumstances surrounding your employment and separation from the Company. For purposes of this Letter Agreement, the term "disparage" shall mean any oral or written statement or representation which, directly or by implication, tends, in the minds of a reasonable

audience, to create a negative impression about the subject of the statement or representation, and includes, without limitation, comments or statements to the press and/or media, including, but not limited to, print journalists, press interviews or statements, newspapers, radio, television, cable, satellite programs, or Internet media (including blogs, web pages, web posts, email, and or "chat programs"), or to the Company, its officers, directors, employees, affiliates, customers, clients, or any person or entity with which the Company has a business relationship which would: (a) adversely affect in any manner the conduct of the business of the Company or the Company's business relationships; (b) adversely affect in any manner the business reputation of the Company, its officers, directors, managing members, investors, employees, attorneys, representatives, affiliates, customers, clients, or any person or entity with which the Company has a business relationship; (c) induce or encourage others, to disparage the Company, its officers, directors, managing members, investors, employees, attorneys, representatives, affiliates, customers, clients, or any person or entity with which the Company has a business relationship.

8. Nothing in this agreement shall be construed to prohibit you from reporting possible violations of federal or state law or regulations to any governmental agency or self-regulatory organization, or making other disclosures that are protected under whistleblower or other provisions of any applicable federal or state law or regulations. You are not required to notify the Company of any such communications; provided, however, that nothing herein authorizes the disclosure of information you obtained through a communication that was subject to the attorney-client privilege. Further, nothing contained in this Letter Agreement shall prohibit you from filing a charge with, or participating in any investigation or proceeding conducted by, the EEOC, or other federal, state or local fair employment practices agency, except that you understand and agree that you will not be able to recover monetary or equitable relief of any kind from Releasees in connection with any such charged filed by you or on your behalf in connection with any action filed by a third party with respect to the claims you are waiving in this Letter Agreement. Additionally, nothing in this Letter Agreement shall constitute a waiver of claims arising after the date you sign it; claims that cannot be waived by law; any right to make any disclosure to or cooperate with the United States Securities and Exchange Commission ("SEC") pursuant to Section 21F(b) of the Securities and Exchange Act or to receive a reward from the SEC in connection therewith; claims for accrued, vested benefits under any employee pension plan of the Company in accordance with the terms of the official plan documents and applicable law; claims for reimbursement through the Company's Flexible Spending Account Program; claims for benefits under the Company's group medical, vision and dental and disability plans in accordance with the terms of such plans and applicable law; or any rights you may have to indemnification under the Company's Certificate of Incorporation and by-laws, any applicable Directors and Officers insurance policy, written indemnification agreement with the Company and any applicable laws (recognizing that such indemnification is not guaranteed by this Letter Agreement and shall be governed by the instrument or law, if any, providing for such indemnification).

9. Notwithstanding your confidentiality and nondisclosure obligations, you are hereby advised as follows pursuant to the Defend Trade Secrets Act: “An individual shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret that (A) is made (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal. An individual who files a lawsuit for retaliation by an employer for reporting a suspected violation of law may disclose the trade secret to the attorney of the individual and use the trade secret information in the court proceeding, if the individual (A) files any document containing the trade secret under seal; and (B) does not disclose the trade secret, except pursuant to court order.”

10. You agree to return to the undersigned immediately upon request, but in no event later than the Separation Date, all property of the Company and/or any of the other Releasees that you have, including but not limited to records and materials, business and client information and files, cardkey access to Company offices, remote access card, desktop and laptop computer, keys, and corporate credit cards, but with the exception of the Company Cellphone, as set forth above.

11. You acknowledge that apart from the payments and benefits that will be provided to you as set forth in this Letter Agreement, you have received all compensation, wages, bonuses, severance or termination pay, stock options, restricted stock units, equity grants, commissions, notice period, leave and/or benefits to which you may have been entitled to under any law, policy or plan of or sponsored by the Company, or pursuant to any prior agreement with the Company and that no other payments or benefits are due or owing to you except as set forth in this Letter Agreement, including any severance payment or benefits under the Severance Agreement or the Offer Letter. You further affirm that you have had no known workplace injuries or occupational diseases.

D. **Mutual Understandings**. The parties mutually agree to the following provisions:

1. It is the Company’s policy not to provide the reasons for any employee’s departure unless required by law. Therefore, any prospective employer who makes an inquiry to the Human Resources Department about your employment shall contact the Company’s Head of Human Resources or her designee, who will confirm only the dates of your employment, the positions you held, and your compensation (provided that compensation information will be provided only if you submit written authorization releasing this information to the Company’s Head of Human Resources or her designee or to the extent required by subpoena, court order or law).

2. Notwithstanding the foregoing Paragraph D.1, nothing herein shall limit the Company’s ability to make any disclosures required by the securities laws or the rules and regulations of the SEC or of any stock exchange on which the Company’s

shares are listed, including (a) the filing of a Current Report on Form 8-K to disclose the fact of your separation and the financial arrangements memorialized hereby , (b) the inclusion of information regarding compensation paid to you as required in any filing with the SEC made by the Company and (c) the filing of this Agreement as an exhibit to the Company's periodic reports filed pursuant to the Securities Exchange Act.

3. Nothing herein is intended to or shall be deemed to constitute an admission that the Company or any of the other Releasees have violated any federal, state or local law (statutory or decisional), ordinance or regulation, breached any contract, or committed any wrongdoing whatsoever against you or otherwise. Neither this Letter Agreement nor any of its terms may be used as an admission or introduced as evidence as to any issue of law or fact in any proceeding, suit or action, other than an action to enforce this Letter Agreement. Moreover, by signing this Letter Agreement you acknowledge that you are not aware of any wrongdoing or fraudulent or unlawful conduct on the part of the Company or the Releasees.

4. In the event that any provision of this Letter Agreement is held to be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions will not in any way be affected or impaired thereby. Moreover, if any provision contained in this Letter Agreement is held to be excessively broad as to duration, scope, activity or subject, that provision will be construed by limiting and reducing it so as to be enforceable to the maximum extent compatible with applicable law.

5. This Letter Agreement, together with any attachments and exhibits hereto, constitutes the entire agreement between you and the Company with respect to the subject matter hereof and supersedes all prior negotiations, representations or agreements relating thereto, whether written or oral, with the exception of any agreements or portions thereof expressly described herein as imposing continuing rights and obligations. You represent that in executing this Letter Agreement, you have not relied on any representation or statement not set forth herein. No amendment or modification of this Letter Agreement shall be valid or binding upon the parties unless in writing and signed by both parties.

6. This Letter Agreement will be governed by and construed in accordance with the laws of the State of New York, except as may be preempted by federal law. This Letter Agreement is binding upon, and shall inure to the benefit of, the parties and their respective heirs, executors, administrators, successors and assigns.

E. **Obligations Unrelated to This Letter Agreement**. Regardless of whether you sign this Letter Agreement, you and the Releasees will have the following rights and obligations:

1. You will be paid for your final wages accrued through the Separation Date and for all accrued vacation days that remain unused as of the Separation Date, with such payment occurring within the time permitted by applicable law.

2. Your participation in the Company's 401(k)/retirement plan(s) will cease on the Separation Date. You will receive any accrued vested benefits under this plan(s) in accordance with the terms of the plan and applicable law. Separate information will be given to you regarding these benefits

3. Your group medical and dental coverage will continue through the last date of the month in which your Separation Date occurs. You will be given separate information regarding your right to continue your group health/dental/vision coverage, as required by COBRA. In the event you do not sign this Letter Agreement, you may elect such continuation coverage, but the coverage would be solely at your own cost without reimbursement from the Company for any part thereof. All COBRA rights are subject to your completion and submission of the proper forms in the times allotted.

4. Pursuant to their terms, any stock option and restricted stock unit awards granted to you by the Company that are unvested as of the Separation Date will terminate effective as of such date. Any outstanding stock option awards granted to you by the Company that are vested as of the Separation Date will remain exercisable for a period of three (3) months from your Separation Date (but no later than the final exercise date (as described in any applicable agreement governing the stock option award).

F. **Consideration and Revocation Periods.** By signing this Letter Agreement in the space provided below and returning it to the undersigned, you are confirming your acceptance of the terms and conditions set forth herein, and you are acknowledging the following:

1. The obligations as set out in this Letter Agreement represent a complete waiver and release of all rights and claims that you have or may have against the Releasees, as provided in Paragraph C.1 above. Accordingly, you should review it carefully before signing it. Likewise, the Reaffirmation attached as Exhibit A reaffirms this waiver and release as of the date you sign the Reaffirmation.

2. You are being provided with at least twenty-one (21) days from your receipt of this Letter Agreement to consider its meaning and effect and to determine whether or not you wish to enter into it, and to consider the meaning and effect of the Reaffirmation and determine whether or not you wish to enter into it. You are advised to consult with an attorney of your choice before signing this Letter Agreement and the Reaffirmation

3. To accept this Letter Agreement and the Reaffirmation you must timely sign each one and deliver each to **Amy Sheehan**, at the address above.

4. By signing this Letter Agreement, you acknowledge that you are receiving consideration beyond that to which you would otherwise be entitled. You further

acknowledge that you have carefully read this Letter Agreement in its entirety, you have had an opportunity to consider the terms of this Letter Agreement for at least twenty-one (21) days, you fully understand the significance of all the terms and conditions of this Letter Agreement and have had a reasonable opportunity to discuss them with an attorney of your choice, and you are signing this Letter Agreement voluntarily and of your own free will and agreeing to all the terms and conditions contained herein.

5. In addition, you may take seven (7) days after signing this Letter Agreement to revoke your signature (such period, the "Letter Agreement Revocation Period"). This Letter Agreement will not become effective until after you sign this Letter Agreement and the Revocation Period expires without revocation (the "Agreement Effective Date"). Any revocation of this Letter Agreement must be in writing and delivered personally or by overnight courier to **Amy Sheehan**, in which event this Letter Agreement will become null and void and your employment with the Company will terminate immediately.

6. You acknowledge that you received this Letter Agreement on January 5, 2018. You understand that this Letter Agreement shall be of no force or effect, and that you shall not be eligible for the consideration described herein, unless you sign and return this Letter Agreement on or before January 27, 2018, and do not revoke your acceptance during the Letter Agreement Revocation Period. Further, you acknowledge that you will not be eligible to receive the payments and benefits described in Paragraph B above unless you also sign and return the Reaffirmation (i) on, but not before, the Separation Date (if the Separation Date is after January 27, 2018, or (ii) no earlier than the Separation Date, but no later than January 27, 2018, and do not revoke your Reaffirmation in the subsequent seven (7) day period (such period, the "Reaffirmation Revocation Period") (the day immediately following expiration of such revocation period is the "Reaffirmation Effective Date").

We wish you the best in your future endeavors.

Sincerely yours,

/s/ Amy R. Sheehan

Amy Sheehan
Senior Vice President & Chief Human Resources Officer
Ophthotech

I hereby agree to the terms and conditions set forth above. I understand that the payments and benefits described in Paragraph B are conditioned upon my timely execution, return and non-revocation of the Reaffirmation.

Agreed to and Accepted by:

/s/ Barbara A. Wood_____
Barbara A. Wood

Date: 5 January 2018

Exhibit A

Reaffirmation of Letter Agreement

I hereby reaffirm as of the date below my agreement to the terms and conditions set forth in the Letter Agreement dated January 5, 2018 between me and the Company (the "Letter Agreement") to which this Reaffirmation is attached as Exhibit A, including, without limitation, the release of claims set forth in Paragraph C thereof. I also agree and acknowledge that apart from the payments and benefits that will be provided to me as set forth in the Letter Agreement, I have received all compensation, wages, bonuses, severance or termination pay, stock options, restricted stock units, equity grants, commissions, notice period, leave and/or benefits to which I may have been entitled under any law, policy or plan of or sponsored by the Company, or pursuant to any prior agreement with the Company and that no other payments or benefits are due or owing to me except as set forth in the Letter Agreement. I further affirm that I have had no known workplace injuries or occupational diseases. I further confirm that I have complied with all of the provisions of the Letter Agreement to date.

By signing hereunder, I acknowledge that I have had a chance to consider this Reaffirmation for at least twenty-one (21) days, that I fully understand the significance of this Reaffirmation and have been advised in writing to discuss it with an attorney of my choice, and that I am signing this Reaffirmation voluntarily and of my own free will. In addition, I understand that I may take seven (7) days after signing this Reaffirmation to revoke my signature, and that this Reaffirmation will not become effective until after I sign it and the Reaffirmation Revocation Period (as defined in the Letter Agreement) expires without revocation.

I hereby provide this Reaffirmation as of the date below and acknowledge that the execution of this Reaffirmation is in further consideration of the payments and benefits that will be provided to me as set forth in the Letter Agreement, to which I acknowledge I would not be entitled if I did not enter into this Reaffirmation. I intend that this Reaffirmation become binding upon me if I do not revoke my acceptance in seven (7) days.

_____ _____

Barbara A. Wood Date

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-219656) pertaining to the 2013 Stock Incentive Plan of Ophthotech Corporation effective August 3, 2017,

(2) Registration Statement (Form S-8 No. 333-211916) pertaining to the 2016 Employee Stock Purchase Plan of Ophthotech Corporation effective June 8, 2016,

(3) Registration Statement (Form S-8 No. 333-208893) pertaining to the 2013 Stock Incentive Plan and Inducement Stock Option Grant of Ophthotech Corporation, effective January 6, 2016,

(4) Registration Statement (Form S-8 No. 333-202438) pertaining to the 2013 Stock Incentive Plan and inducement stock options of Ophthotech Corporation, effective March 2, 2015,

(5) Registration Statement (Form S-8 No. 333-193694) pertaining to the 2013 Stock Incentive Plan of Ophthotech Corporation, effective January 31, 2014,

(6) Registration Statement (Form S-8 No. 333-191767) pertaining to the 2013 Stock Incentive Plan and Amended and Restated 2007 Stock Incentive Plan of Ophthotech Corporation, effective October 16, 2013,

of our reports dated March 5, 2018, with respect to the financial statements of Ophthotech Corporation, and the effectiveness of internal control over financial reporting of Ophthotech Corporation included in this Annual Report (Form 10-K) of Ophthotech Corporation for the year ended December 31, 2017.

/s/ Ernst & Young LLP

MetroPark, New Jersey

March 5, 2018

Exhibit 31.1

CERTIFICATIONS

I, Glenn P. Sblendorio, certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2017 of Ophthotech Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

    a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

    a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

    b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 5, 2018

By: /s/ Glenn P. Sblendorio

Glenn P. Sblendorio

Chief Executive Officer

(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, David F. Carroll, certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2017 of Ophthotech Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 5, 2018

By: /s/ David F. Carroll

David F. Carroll
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Ophthotech Corporation (the "Company") for the fiscal year ended December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Glenn P. Sblendorio, Chief Executive Officer of the Company, hereby certifies, pursuant to Rule 13a-14(b) and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 5, 2018

By: /s/ Glenn P. Sblendorio

Glenn P. Sblendorio
Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Ophthotech Corporation (the "Company") for the fiscal year ended December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, David F. Carroll, Chief Financial Officer of the Company, hereby certifies, pursuant to Rule 13a-14(b) and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 5, 2018

By: /s/ David F. Carroll

David F. Carroll
Chief Financial Officer
(Principal Financial Officer)